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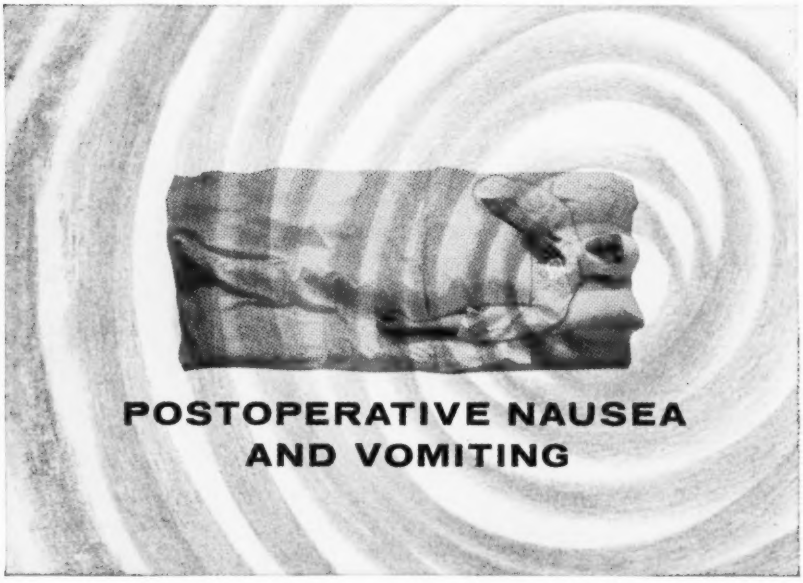

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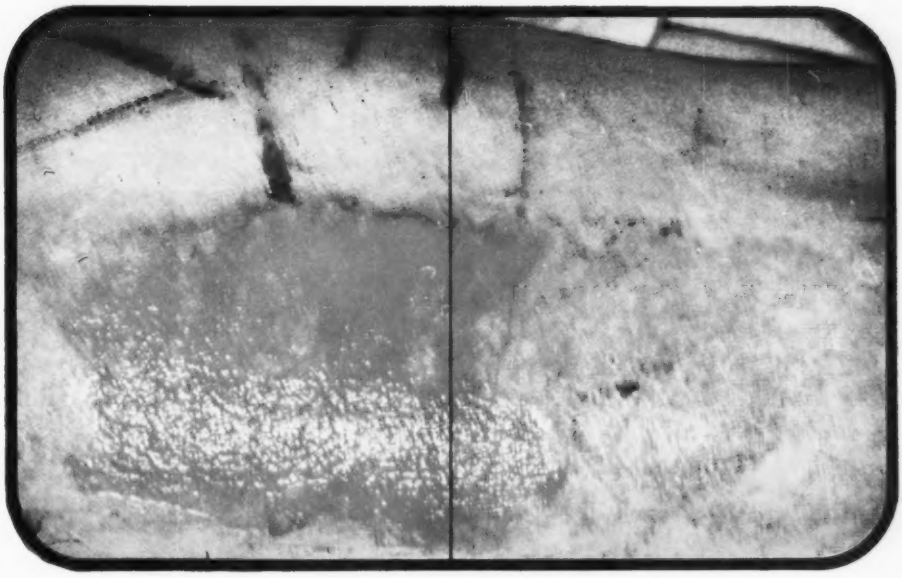

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[1]Thomson, J. E. M.: Am. J. Surgery 91:413 1956

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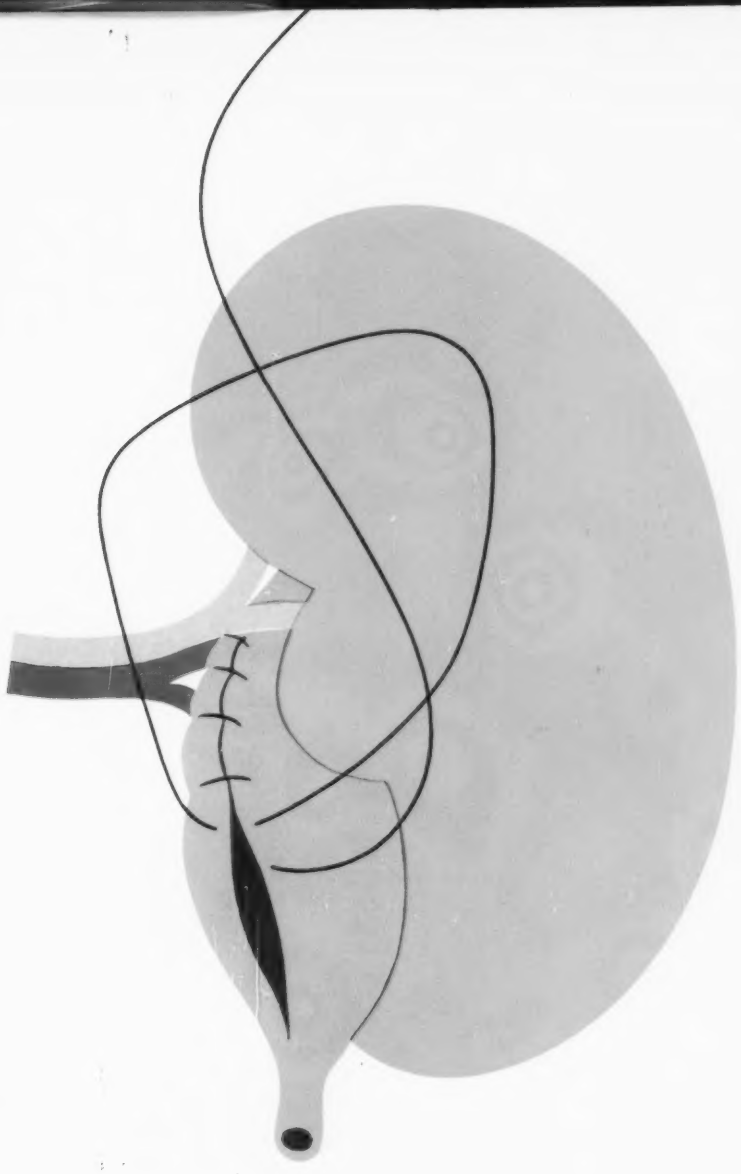

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Peptic Ulceration in Childhood

WILLIAM L. CRAVER, M.D., and FRANK GLENN, M.D., New York

Certain disease entities and conditions commonly encountered among adults may also be found in the very young. Generally youth seems to resist them, but once established they tend to persist and increase in extent. Peptic ulcer is prevalent among adults in this country. Readily recognized, it is well treated, so that it is estimated that 85% of patients properly diagnosed are managed satisfactorily by medical treatment and less than 15% require surgical therapy. By comparison, peptic ulcer is considered very rare in children. Because of its seeming infrequency, it is seldom mentioned in the differential diagnosis of gastrointestinal disease in the very young. During a review of the cases of adult patients with peptic ulcer, we became impressed with how often the history of the disease extended back into early childhood. Abdominal pain and other symptoms compatible at least with ulcer have been common among those who have been the most difficult to manage by either medical or surgical therapy. Although we are undecided concerning the significance of this observation, it has stimulated us to review our experience with children in whom peptic ulcer has been demonstrated in an attempt to determine what their subsequent course has been. If the appearance of a peptic ulcer in early life is an indication of a severe ulcer diathesis, then it is important to seek out such patients for study and treatment.

Submitted for publication June 23, 1958.

From the Department of Surgery, the New York Hospital-Cornell Medical Center (21).

Occasional articles on peptic ulceration in adults mention the fact that some adults with gastric or duodenal ulcerations are able to recall symptoms dating back to childhood. Proctor [1] examined the records of 1000 patients with gastric ulcers and 1000 with duodenal ulcers. Sixteen of the former and twenty-six of the latter recalled symptoms when they were children. It is rare to find a report which approaches the problem from the opposite direction. Following the clinical course of children with peptic ulcers for several years, and even into adult life, will surely add to our understanding of this disease process.

At the New York Hospital-Cornell Medical Center, a patient who developed ulcer symptoms at the age of 12 was followed until he reached the age of 31. Over a 25-year period, 1932-1957, nine other children with peptic ulceration were observed in the New York Hospital, and these were followed for shorter periods, ranging from one year three months to eight years. In addition, another child with duodenal ulcer died in infancy.

In addition to the 11 patients with primary peptic ulceration, 6 children developed an ulcer in association with some other serious disease or while receiving steroid therapy. These cases are not included in the present report.

Incidence

The incidence of 11 cases of primary peptic ulceration in children in approxi-

	Age at Diagnosis	Sex	Symptoms	Duration	Ulcer Location	Treatment	Follow-Up
A. Neonatal							
No cases							
B. Infantile							
Case 1	6 wk.	M	Presistent vomiting	3 days	Duodenum	Medical	Septic course; death
C. Early childhood							
Case 2	2 yr. 9 mo.	F	Vomiting after meals	1 mo.	Pyloric or prepyloric	Medical	Three additional episodes of pyloric obstruction in 4 yr.
D. Late childhood							
Case 3	15 yr.	M	2 episodes of G. I. bleeding	3 yr.	Duodenum	Subtotal gastrectomy	3 yr. later—vagotomy for marginal ulcer
Case 4	10 yr. 6 mo.	M	Hematemesis, epigastric pain	3 yr. 8 mo.	Duodenum	Pyloroplasty & vagotomy	2 yr. 5 mo. later—excellent result
Case 5	11 yr.	M	Abdominal pain	1 mo.	Duodenum	Medical	8 yr. later—asymptomatic
Case 6	11 yr.	F	Epigastric pain	10 yr.	Duodenum	Medical	5 yr. later—occasional vomiting
Case 7	12 yr.	M	Hematemesis, vomiting, pain	4 yr.	Duodenum	Medical	7 yr. later—asymptomatic
Case 8	15 yr.	M	Hematemesis, epigastric pain	2-3 yr.	Duodenum	Medical	2 yr. later—recurrence of pain
Case 9	15 yr. 5 mo.	M	Hematemesis, pain, vomiting	4 yr. 4 mo.	Duodenum	Medical	3 yr. 7 mo. later—asymptomatic
Case 10	16 yr. 2 mo.	F	Abdominal pain	9 yr.	Duodenum	Medical	1 yr. 3 mo. later—occasional pain
Case 11	16 yr. 9 mo.	M	Rectal bleeding, epigastric pain	1 yr. 6 mo.	Duodenum	Medical	Tarry stools once in 5 yr.

mately 480,000 total hospital admissions is consonant with that reported by others.[1,2] Approximately 1750 operative procedures for peptic ulceration have been performed on the pavilion service of the New York Hospital from 1932 to 1957. During this 25-year period two young patients, one 17 years old and one 10½ years old, were operated on for duodenal ulcers. The rest of the 11 children had a medical regimen.

Classification

Primary peptic ulcerations in children may be classified by age and symptomatology[3,4] (Table).

A. Neonatal.—It has long been recognized that children in the neonatal period (0-14 days) may have sudden, acute, fulminating symptoms without recognizable premonitory signs. The majority have bleeding or perforation or both. There are no cases of this type in the present series.

B. Infantile.—In the infantile period (15 days to 1 year) there often are premonitory signs, such as refusal of feeding, vomiting, or abdominal pain. The majority have bleeding or perforation, but persistent pylorospasm or cicatricial pyloric stenosis is occasionally seen. Many are septic and marasmic. Because of their poor general condition, few of these patients are operated on. In some the symptoms subside, and health returns.

CASE 1.—One of the patients treated at the New York Hospital was 6 weeks old at the time of diagnosis. Three days before admission vomiting began and persisted. He had eaten well until this time but then lost weight steadily. After admission watery diarrhea began. After initial improvement, a septic course began and soon led to death. At autopsy a punched-out ulcer, 5 mm. in diameter, was demonstrated in the duodenum just beyond the pylorus. Microscopically the ulcer extended almost through the bowel wall, and the margins were infiltrated with inflammatory cells. There was mild congestion of the jejunal mucosa, but intestinal cultures were negative for pathogens.

C. Early Childhood.—In the early childhood group (one to nine years of age) only occasional cases are recognized. The symptoms are more chronic and include vague gastrointestinal complaints, failure to gain weight, and abdominal pain. Hemorrhage, perforation, or stenosis occurs less frequently. In the present series one patient is in this age group.

CASE 2.—This girl was 2 years 9 months old at the time of diagnosis. One month earlier she had begun to vomit after meals. This became increasingly frequent. On admission marked peristaltic movements could be traced from the left to the right side of the upper abdomen. Roentgenograms demonstrated a dilated stomach and a pyloric-canal or prepyloric ulcer. Free hydrochloric acid was present in the fasting gastric secretion. She improved with medical therapy and was discharged. During the next four years she had three additional episodes of partial pyloric obstruction. Her subsequent course is not known.

D. Late Childhood.—Patients in the late childhood group have a disease process which approaches that found in adults. Symptoms may be present intermittently or continuously for months or years. The remaining nine patients of the series belong in this group. They vary in age at diagnosis from 10½ years to 16 years 9 months. Hematemesis or rectal bleeding preceded admission in six of the nine. The other three had abdominal pain. One child had had pain since the age of one year (Case 5). The duration of symptoms ranged from 1 month to 10 years, with a mean of 3 years 8 months. Seven of the patients in this group were boys and two girls. This is in keeping with the known preponderance of peptic ulceration in males of all ages. Even in the newborn, males outnumber females, but not strikingly so. Bird[3] found the ratio of males to females to be approximately 1.5:1 in a group of 243 cases.

The diagnosis was established radiographically in all patients. In two, discussed below, operation confirmed the diagnosis. All the ulcers in the late childhood group were located in the duodenum. Duodenal ulcers are several times commoner than gastric ulcers in children.[2,3]

Gastric analysis was performed in five patients. In each, free hydrochloric acid was present in the fasting specimen and a rise occurred after histamine stimulation.

Two in the late childhood category had definitive operative treatment for primary

duodenal ulceration. The following case history is of interest because the patient was followed until 31 years of age.

CASE 3.—This boy developed upper abdominal pains and vomiting when 12 years old. An appendectomy was done, but symptoms persisted intermittently. Three years later hematemesis occurred and roentgenograms showed a duodenal ulcer. Hematemesis recurred at 16, and he was admitted. Conservative measures again improved his condition, but one year later he was readmitted with pyloric obstruction. A subtotal gastric resection was done, and a small ulcer on the posterior wall of the first part of the duodenum was found. He did well and remained asymptomatic during Army service. After discharge, three years postoperatively, epigastric pains and vomiting developed. A marginal ulcer was demonstrated at another hospital. A transthoracic vagotomy was performed at age 21. He is now 31 years old, and during this 10-year period he has remained free of symptoms, leading a full, normal life, and currently weighing 200 lb.

The second operative case has been followed for a shorter period.

CASE 4.—This boy developed epigastric pains before meals when 10½ years old. A duodenal ulcer was shown radiographically. He improved on a medical regimen but continued to have occasional symptoms for three years. Nausea, hematemesis, and bloody bowel movements preceded his admission. Bleeding ceased after transfusions. An active ulcer was again demonstrated. At operation the ulcer was found in the anterior duodenal wall. A pyloroplasty and vagotomy were done. He has been followed for two years five months (to age 16½), and he has been asymptomatic.

The remaining seven patients were treated medically. Three have been symptom-free in the follow-up period; three have had occasional abdominal pain or vomiting, and one had an episode of rectal bleeding during his five-year follow-up.

Comment

Only three of the children with peptic ulceration have remained asymptomatic during their period of observation. Seven others have had recurring or persistent symptoms, which have been partially controlled by medical management. Two of these required operative treatment for relief of symptoms. One child was treated by pyloroplasty and vagotomy. Another underwent transthoracic vagotomy three years after a subtotal gastric resection.

Some of the patients managed medically may eventually need operative treatment. Only long-term follow-up study will elucidate this. Extended follow-up reports of children with peptic ulceration are rare in the literature. We are unaware of any reports in which children have been followed into adulthood. The 16-year study of the boy who had a gastric resection (Table; Case 3) is, therefore, unique.

Johnson, Sleisenger, and Beal[5] have shown that the recurrence rate in the young adult who is subjected to operation for duodenal ulcer is higher than that usually associated with these operations. Perhaps the same holds true in the child. These considerations suggest that the ulcer diathesis may be severer in children who develop peptic ulceration. However, to confirm this assumption, additional children will have to be followed into adult life.

Summary

Eleven cases of primary peptic ulceration in children are presented. Six of the children had episodes of gastrointestinal hemorrhage. Two patients were operated on, and one was followed for 16 years.

Additional long-term follow-up studies of children with peptic ulceration are desirable to determine whether the ulcer diathesis is indeed severer in the young patients.

New York Hospital, 525 E. 68th St. (21).

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Favorable Postgastrectomy Results in Billroth II Patients with a Small Stoma

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The authors report a clinical experiment conducted over a course of six years presenting evidence that favors the small, but not too small, stoma, and shows that better results are thereby accomplished. We therefore do not need to use the Billroth I operation.

The Billroth II type of gastric resection has been largely accepted by surgeons for its ability to prevent peptic ulcer recurrence if definitive operation is required. The recurrence rate is the lowest for all procedures, and the mortality and immediate morbidity rates are comparable. However, the late postgastrectomy findings of weight loss, diarrhea, and the dumping syndrome with accompanying weakness are believed to be more numerous than those with other procedures, notably gastroenterostomy and the Billroth I procedure. These disagreeable sequelae have urged surgeons to find a better operative procedure.[1-12] It is apparent that if the postgastrectomy symptoms could be prevented or materially lessened, then the Billroth II procedure should be the best available operation as we know gastric surgery for ulcer today.

When one studies the postoperative Billroth II patients, the idea immediately appears that the symptoms must be due to loss of the pyloric sphincter and stomach, which is usually associated with rapid emptying of the stomach. This sudden flow of food and fluid into the jejunum, then, must be slowed if the symptoms are to be bettered. Obviously, stomach loss must be had if a form of resection is employed.

Present Study

To test the validity of this concept, we set up a clinical experiment in which deliberate formation of a small stoma was accomplished in the Billroth II operation. The purpose of the small size of the stoma was an attempt to slow the gastric emptying. Roughly, 1.5 to 2.5 cm. has been the selected size of the small stoma, although this cannot be accurately measured. In this study, a stoma of 2.5 to 6 cm., or larger, is recognized as large. We have been able to measure some large stomata of the Polya type of gastrectomy and have found the anastomosis to be 4 to 6 cm. in diameter. The small stoma is measured by one finger by some operators, or a finger tip and a half by others, and this measures roughly 1.5 cm. Admittedly, this method is not scientifically accurate, but the use of the finger and thumb to measure gastrointestinal anastomoses is a part of a surgeon's trade; the method is employed daily and can be considered worthy of consideration. It is enough to the experienced surgeon, we believe, to state whether the stoma is small (1.5 cm., more or less) or large (3 to 8 cm.) and that these observations are accurate enough to be meaningful.

This study compares the postgastrectomy results in 100 patients with small stomata and those in 100 patients with large stomata. We narrowed the gastrojejunal stoma to a diameter of 1.5 to 2.5 cm., hoping to achieve partial obstruction in 100 Billroth II gastrectomies to test this theory. For a control group, 100 identical gastrectomies, except for the large stomata (measuring 4 to 8 cm. in diameter), were used. Approximately 65% of the stomach was removed, and the

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TABLE 1.—*Data on Small- and Large-Stoma Patients*

Group	Average Age, Yr.	Average Follow-Up, Mo.	Vagotomy, %	No. Patients
Small stoma	46.3	31.9	52	100
Control	43.5	40.5	44	100

jejunum was placed either anti- or isoperistaltically. All anastomoses were retrocolic, and vagotomies were included in young patients or patients with high gastric acidity. The two series of experiments were performed concurrently during a period of six years. Both series represent consecutive cases in which personal follow-up interviews were obtained. In all, 114 small-stoma gastrectomies were performed, but 14 were lost in follow-up studies. The two groups appear similar, as noted in Table 1.

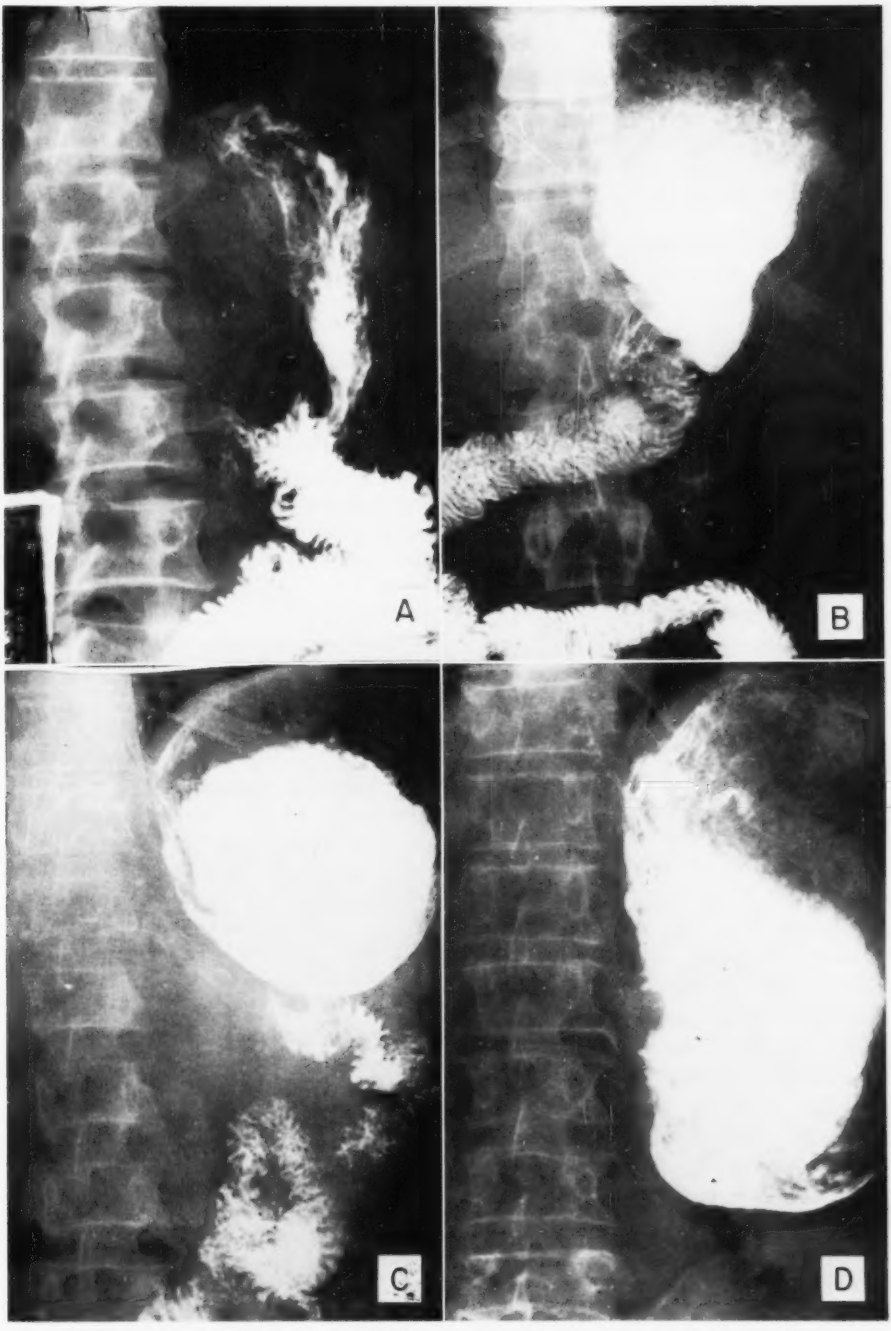
For the sake of clarity, we refer to all unpleasant symptoms which are generally recognized as being the result of the resection procedure as "postgastrectomy symptoms," referred to above. The so-called abnormal afferent-loop filling[13] was exceedingly rare in our postoperative study of nearly 700 gastrectomized patients.

Many surgeons have noticed a reduced incidence of the postgastrectomy syndrome in patients who have a small stoma between the stomach and the jejunum.[14-23] Sawyer[24] has recommended reduction of the size of the gastrojejunostomy stoma to 1½ fingerbreadths in patients with a severe dumping syndrome. Some authors emphasize the importance of a valve action at the gastrojejunostomy stoma to lessen proximal-loop filling and postgastrectomy discomfort.[25-32] It should be noted that these valvular stomata are usually associated with a small stoma because the lesser-curvature portion of the gastric pouch is inverted for the valve. Of special interest is a report by Porter[33] of 118 gastrectomies, Billroth II type, in which he employed a stoma measuring 2.5 cm. in diameter to avoid the dumping syndrome. The stoma was made small enough to produce purposely a partial obstruction of the stoma and thereby cause a slow gastric emptying that could be definitely measured by postoperative roentgen studies of the stomach. After the usual Polya variety of gastrectomy, gastric emptying usually takes place within a period of 20 minutes, using the gastric fluid level as an index,[34] but with the small stoma the fluid level in the stomach did not disappear for an average of 57 minutes. Porter[33] reports a reduction in the incidence and severity of the dumping syndrome in the small-stoma cases. Goligher[35] reports failure to avoid the dumping syndrome in six cases with small stomata, but roentgen studies of the stomach revealed rapid emptying. Other authors disagree with Porter,[33] and Kennedy[36] states that the jejunal lumen controls the emptying. This is probably true only if the gastrojejunal stoma is larger than the jejunum and is not true in the reverse case, as can clearly be shown in the roentgenograms (Figure, *B* and *C*). Some authors consider the partial stomal obstruction as undesirable.[37-39]

The favorable results reported following the Billroth I gastrectomy may be due to the fact that the gastroduodenal stoma is of necessity small because of the small caliber of the duodenum when an end-to-end anastomosis is performed.[40-42]

Stomal Obstruction.—During the postoperative period the small-stoma gastrectomy patients were observed for stomal obstruction. Before discharge from the hospital, barium visualization of the stomach was carried out, and stomal obstruction could be accurately assessed. The desired amount of stomal obstruction would usually appear as a large, globular gastric pouch with a fluid level and a small stream of barium in the gastrojejunal stoma (Figure, *B* and *C*). A four-hour visualization of the stomach would usually show some retained barium.

According to these criteria, 69 patients showed definite evidence of stomal obstruction, as follows:



Barium roentgen studies of stomach following subtotal gastrectomies. *A*, patient with large stoma (control group) and rapid gastric emptying. *B*, *C*, and *D*, patients with small stomata and moderate, severe, and almost total stomal obstructions, respectively.

TABLE 2.—*Postcibal Symptomatology*

Group	No Symptoms	Mild Atypical Symptoms	Dumping			No. Patients
			Mild	Mod.	Severe	
Small stoma	53	31	10	3	3	100
Control	28	40	18	10	4	100

In 59 patients moderate obstruction was demonstrated (Figure, *B*), and in 7 severe obstruction (Figure, *C*), which required gastric decompression and lengthened hospitalization, was shown. Three patients had so nearly total obstruction by the deliberately formed small stoma (Figure, *D*) that reoperation and enlargement of the stoma were required. The results in two of these patients are excellent, but the third patient showed no improvement.

Thirty-one patients showed no definite evidence of stomal obstruction during the postoperative period (Figure, *A*).

Results

Follow-up studies by personal interview revealed that the postgastrectomy syndrome was reduced approximately by one-half in the small-stoma group as compared with the control group (Table 2). Weight loss was reduced from an average of 9.83 lb., in the control group, to 3.84 lb., in the small-stoma group. Weakness, which seemed to be the commonest and severest complaint of the control group, was decidedly better in the small-stoma group. Interestingly, diarrhea was approximately equal in frequency in the two groups (Table 3).

Comment

Subtle distinction in postcibal symptomatology in the two groups did not seem feasible in this series. If there was doubt about the presence of postgastrectomy symptoms, we used the oral glucose intake test (250 cc. of 50% dextrose by mouth), which proved to be very practical and produced the proper symptoms if the patient had really experienced the postgastrectomy syndrome.[43] It was often difficult to separate psychosomatic symptoms from the actual ones, but the glucose test was quite helpful in these instances.

However, we are convinced that a small number of patients experienced the dumping syndrome even when stomal obstruction was present. It is well known that certain persons can so well adjust themselves by diet and fluid intake that the postgastrectomy symptoms are greatly minimized, even to the point where it is difficult to know that the symptoms are significant.

In this study, the main difficulty was the technical aspect of making the partially obstructing gastrojejunal stoma. At the end of the operation, the surgeon often could not predict the degree of stomal obstruction that would follow. The best results were obtained from stomata that would just admit one small finger, but since there was no way to measure the size accurately upon completion of the anastomosis, the experience and judgment of the surgeons were quite important. The three cases in which the stomata were too small and the obstruction had to be released by a second operation occurred early in our experience, and we have obtained confidence in the procedure and do not expect this to recur in the future.

TABLE 3.—*Incidence of Weakness and Diarrhea in Small- and Large-Stoma Groups*

Group	Weakness			Diarrhea			Average Weight Change	No. Patients
	None	Mild	Severe	None	Mild	Severe		
Small stoma	81	16	3	81	15	4	3.84 lb. (loss)	100
Control	68	11	21	82	16	2	9.83 lb. (loss)	100

The late hypoglycemia syndrome, proximal-loop filling, and jejunal dilatation were less troublesome in the small-stoma group.

One postgastrectomy patient with a marked dumping syndrome and a large stoma was reoperated upon and the stoma narrowed to one-finger size. On follow-up visit, five months later, the patient expressed himself as delighted. There was no evidence of the dumping syndrome or of any other postgastrectomy symptoms. He had gained 10½ lb. in weight. There is no weakness, and he partakes heavily of the foods and fluids known to produce the dumping syndrome prior to this revision.

Summary

The postgastrectomy symptoms following the Billroth II gastrectomy are a serious problem.

The etiology of the postgastrectomy syndrome is closely related to rapid gastric emptying.

Creation of a partially obstructing small gastrojejunal stoma appeared to be a practical method of avoiding rapid gastric emptying following Billroth II gastrectomy in at least 75% of patients receiving the small stoma.

Follow-up studies were performed on 100 small-stoma and 100 large-stoma patients receiving Billroth II gastrectomies.

These studies reveal a definite reduction in the postgastrectomy syndrome in the small-stoma as compared with the large stoma group.

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Emergency Surgery for Severe Upper Gastrointestinal Hemorrhage

An Analysis of Sixty-Four Cases

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Introduction

This report considers only those patients who were operated upon as emergencies because of severe upper gastrointestinal bleeding. The case series was accumulated in the years 1950 through 1957, at a large Army hospital and includes active-duty military personnel and their dependents, retired military personnel, and Veterans' Administration beneficiaries. Not included are the many patients whose bleeding ceased with conservative treatment or those persons who were operated upon electively after a bleeding episode.

Since management of this type of bleeding problem varies in different centers, the approach employed at this hospital is described, in addition to the indications for surgical intervention, details of the surgical procedures employed, and the results obtained by surgery.

Combined Medical-Surgical Approach to Upper Gastrointestinal Bleeding

A combined medical-surgical evaluation of this type of bleeding has been advocated, practiced, and reported previously.[1,5,8] At this center such a program has been in effect for several years, although several changes in chiefs of Surgery and Gastroenterology have occurred by routine reassignment. As a result all patients operated upon were subjected to surgery only after consideration by, and common consent of, these services. Such unanimity of opinion between services is by no means automatic and is most usually achieved only after considerable observation and discussion of the particular case in question. We believe, however, that such evaluation and decision are more apt to serve the best interests of this group of patients than a unilateral opinion of either of the services alone.

The plan of treatment may, for the purpose of this discussion, be divided into three phases: resuscitative, diagnostic, and therapeutic. In actual practice, these phases blend to form an uninterrupted program. The resuscitative phase begins when the patient is admitted to an emergency ward, staffed and equipped to handle this type of patient. Senior members of the Surgery and Gastroenterology Services are notified; the patient is examined, and a history taken and blood specimens drawn for typing and cross matching, and for hemogram and blood chemistry if indicated. At the same time, intravenous infusions of appropriate fluid are started in two or more locations with large-bore needles, nasogastric suction is instituted, an indwelling catheter placed, and urine obtained for analysis. A bedside chart is established to provide a current record of vital signs, fluid therapy, and medications given.

The diagnostic phase begins when the patient's clinical condition has stabilized sufficiently to permit lavage of the stomach with ice water through a F. 30 Ewald tube, followed immediately by esophagoscopy and gastroscopy.[9] While the stomach is still

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relatively free of blood, an emergency upper gastrointestinal series is obtained, along with a chest x-ray. If the patient's bleeding ceases, a medical program begins the therapeutic phase and consists of appropriate medications, diet, and further diagnostic studies. If the patient continues to bleed, surgical treatment is considered, and, if employed, duodenal ulcers, gastric ulcers, and patients with the bleeding site undetermined are usually treated by subtotal gastric resection. Total gastric resection is reserved for those few patients with high gastric lesions whose bleeding cannot be controlled by subtotal resection. After such surgery, the postoperative care consists of appropriate fluids, antibiotics, early ambulation, food by mouth when bowel function is regained, dietary instructions on leaving the hospital, and follow-up appointment in the Gastroenterology Clinic after discharge.

Indications for Surgery

Most internists and surgeons will agree that the majority of patients bleeding from peptic ulceration are best managed conservatively during their acute bleeding phase and, contrariwise, that a minority of patients will require surgical intervention as their only reasonable hope of survival.[2-4,7] How to obtain the best possible over-all results by a proper balance between medical and surgical programs is less clear, and has led some investigators to submit their criteria for surgical management of gastrointestinal bleeding. These have included such factors as the intensity and rate of blood loss, estimated volume of blood loss, a decrease in hemoglobin, hematocrit, or blood volume values to arbitrary minimum levels, recurrence of hemorrhage, the presence of complicating disease, and the very practical consideration of the quantity of blood available for replacement.[1,3-6,8] Our criteria for emergency surgical treatment are flexible, the most important single consideration being the failure to stabilize the patient's clinical condition by vigorous resuscitative measures, regardless of estimated total blood loss, frequency of bleeding, the patient's age, the presence of complicating disease, or laboratory values.

The terms "severe" and "massive" bleeding are difficult to define and would appear valid only in their clinical application, since the loss of a certain volume of blood in a given time may produce in one patient a much more profound physiological effect than the same volume loss in another patient. To avoid serious challenge on this point, only those patients are included in this series whose blood loss was estimated to be in excess of one-half their blood volume, as determined by hematocrit, hemoglobin, and the quantity of replacement required.

Analysis of Series

Basic Data.—The number of patients who entered the hospital with upper gastrointestinal bleeding, during the years 1950 to 1957, inclusive, was 353. The number of patients in this series who were operated upon was 64 (18.1%). Of this group, 12 (18.8%) were on active-duty status; another 12 were retired military personnel members; 4 (6.2%) were military dependents, and 36 (56.2%) were Veterans' Administration beneficiaries. Male patients numbered 62 (96.9%) and women 2 (3.1%). The age extremes in the series were a youthful 17 and a senile 74 years of age. Table 1 shows the number of patients in each age decade and reveals 33 (51.6%) of the group to be below the age of 50 years and 31 (48.4%) to be 50 years of age or more. It is of interest that as many patients required surgery in the 30- to 39-year age group as in the 50- to 59-year age group. Possibly this may be accounted for by the relative concentration of young men in the military service and the large group of World War II veterans authorized care at this hospital.

Table 2 indicates the number of patients operated upon each year and shows a steady increase except for the year 1954.

To check an impression that the fall season of the year is associated with an increase in the number of patients requiring surgery

TABLE 1.—*Number of Surgical Candidates by Age Decade*

Age Group (by Decades)	No. of Patients	Per Cent of Patients
0-9	0	0.0
10-19	2	3.1
20-29	6	9.4
30-39	14	21.9
40-49	11	17.2
50-59	14	21.9
60-69	15	23.4
70-79	2	3.1

TABLE 2.—*Number of Patients Operated upon by Year*

Year	No. of Patients	Per Cent of Patients
1950	3	4.7
1951	4	6.3
1952	5	7.8
1953	10	15.6
1954	4	6.3
1955	11	17.2
1956	12	18.7
1957	15	23.4

for gastrointestinal bleeding, the number of patients operated upon in each quarter of the year was totaled in Table 3, revealing the percentages by quarter.

The month of November alone accounted for 12 (18.8%) of the entire group, in contrast to July, when no operations were done for gastrointestinal bleeding during the entire eight-year period.

TABLE 3.—*Surgery for Gastrointestinal Bleeding by Quarter*

Yearly Quarter	No. of Patients	Per Cent of Patients
January, February, March	15	23.4
April, May, June	8	12.5
July, August, September	16	25.0
October, November, December	25	39.1

Type of Lesions Encountered.—As would be expected, the commonest source of bleeding was from duodenal ulceration. Gastric ulcerations was the second commonest source of bleeding, and in the group of 18 patients with this lesion, 3 were found to have malignant and 15 benign ulcers. In 10 patients the bleeding site was never determined, and details of the postoperative course of this difficult group are furnished in later sections of this paper. Three patients exhibited severe bleeding from stomal ulcers; another patient was found to have a mucosal tear at the gastric cardia, apparently associated with repeated episodes of vomiting (Mallory-Weiss syndrome), and one patient was found to be bleeding from esophageal varices—a condition not recognized preoperatively. Table 4 lists the type and frequency of the lesions found at surgery.

TABLE 4.—*Type and Frequency of Lesions Found at Surgery*

Type of Lesion	No. of Patients	Per Cent of Patients
Duodenal ulcer	31	48.4
Gastric ulcer	18	28.1
Stomal ulcer	3	4.7
Undetermined bleeding site	10	15.6
Other than ulcer		
Esophageal varices	1	1.5
Laceration at gastric cardia (Mallory-Weiss syndrome)	1	1.5

Manifestations of Bleeding.—Considering the entire series as a single group, both hematemesis and melena were recorded in 44 patients (68.8%), melena only in 13 (20.3%), and hematemesis only in 7 (10.0%). Table 5 shows in per cent the manifestation of bleeding according to the type of lesion.

Preoperative Hemoglobin and Hematocrit Values.—These determinations, although of limited accuracy in acutely bleeding patients, are readily obtainable and of value when

TABLE 5.—*Manifestation of Bleeding*

Type of Lesion	No. of Patients	Hematemesis and Melena, %	Melena Only, %	Hematemesis Only, %
Duodenal ulcer	31	71.0	25.8	3.2
Gastric ulcer	18	77.8	5.5	16.7
Stomal ulcer	3	100.0	0.0	0.0
Undetermined site	10	40.0	30.0	30.0
Other than ulcer				
Esophageal varices	1	0.0	100.0	0.0
Laceration, gastric cardia	1	100.0	0.0	0.0

TABLE 6.—*Preoperative Hemoglobin and Hematocrit Values*

Hemoglobin			Hematocrit		
Range, Gm.	No. of Patients *	Per Cent of Patients	Range, Vol. %	No. of Patients †	Per Cent of Patients
3-6	22	35.5	10-20	17	27.8
7-10	37	59.7	21-30	32	52.5
11-13	3	4.8	31-36	12	19.7

* In two cases no hemoglobin determination was recorded.
† In three cases no hematocrit determination was recorded.

interpreted with reservation and in correlation with the clinical findings.[3] (Blood volume determinations have not until the past year been available for emergency clinical use and still require much more time than do standard hematocrit and hemoglobin tests.)

The average of the preoperative hemoglobin values for the entire group was 7.7 gm/100 cc. A similar average of the preoperative hematocrit values was 24.2 vol. %. In Table 6 the percentages of patients falling within arbitrarily selected hemoglobin and hematocrit ranges are presented and probably reflect a more accurate picture of the severity of bleeding than do gross averages alone.

Transfusion Requirements—Whole Blood. The extremes of replacement therapy varied from a minimum of 3000 cc., in three patients, to a maximum of 24,700 cc., in one patient, while the average for the entire group was 7240 cc. per patient. As with the hematocrit and hemoglobin values, the gross average is of little significance, and Table 7 lists arbitrary ranges of transfusion requirements and the percentages of patients within these ranges. Further observation of these figures reveals that 31 (48.4%) of the group required replacement estimated to be one-half to equal blood volume and 33 (51.6%) in the quantity of one to four times the estimated blood volume.

Preoperative Endoscopy.—Esophagoscopy and/or gastroscopy was done as an emergency procedure in 41 (64.1%) of the 64 cases by the staff gastroenterologist or

TABLE 7.—*Transfusion Requirements*

Range, Cc.	No. of Patients	Per Cent of Patients
3000-5900	31	48.4
6000-8900	20	31.3
9000-11,900	3	4.7
12,000-14,900	4	6.2
15,000-25,000	6	9.4

his representative, preferably during the actively bleeding period. The potential dangers inherent in peroral endoscopy are appreciated but no injuries have been recorded, and it is believed that the results are worth the risk in terms of accurate diagnosis and proper direction of therapy. Table 8 presents the findings of these procedures.

Endoscopy of this type may be done in the resuscitative phase when the patient's condition has been moderately well stabilized. It is of value in a negative way in helping to rule out esophageal varices, hiatus hernia, and esophagitis as the source of hemorrhage, and in a positive way by visualizing some of the gastric and stomal lesions. One patient in the series who was operated upon and found to have bleeding esophageal varices had not undergone esophagoscopy. The patient survived, but the laparotomy was obviously ill-timed and inappropriate.

Preoperative X-Ray Findings.—In accordance with the plan of a vigorous resuscitative and diagnostic approach to the problem of gastrointestinal hemorrhage, 52 (81.3%) of the patients had emergency preoperative upper gastrointestinal barium

TABLE 8.—*Preoperative Endoscopy*

Type of Lesion	No. of Patients with Lesions	Per Cent of Patients Examined	Findings, %	
			Negative	Positive
Duodenal ulcer	31	58.1	94.4	5.6 (varices seen)
Gastric ulcer	18	55.6	70.0	30.0
Stomal ulcer	3	66.7	50.0	50.0
Undetermined	10	100.0	100.0	0.0
Other than ulcer				
Esophageal varices	1	0.0	0.0	0.0
Laceration, gastric cardia	1	100.0	0.0	100.0

TABLE 9.—*Preoperative X-Ray Findings*

Lesion Identified at Surgery	Total No. of Patients	Per Cent Patients X-Rayed	Lesion "Seen" on X-Ray	Lesion Not "Seen" on X-Ray
Duodenal ulcer	31	77.4	87.4	12.5
Gastric ulcer	18	77.8	57.1	42.9
Stomal ulcer	3	100.0	66.7	33.3
Bleeding site undetermined	10	100.0	40.0	60.0
Other than ulcer				
Esophageal varices	1	0.0	0.0	0.0
Laceration, gastric cardia	1	100.0	0.0	100.0

studies. The remaining 12 (18.7%) of the patients who did not have such x-ray examinations had either been treated in the early years of the series or had known ulcers demonstrated in the recent past and prior to their bleeding episode. Table 9 presents the findings of these examinations for each type of lesion identified at surgery.

Although no specific lesion could be identified at surgery in 10 patients, preoperative x-ray examination suggested the presence of a false-positive duodenal lesion in 4, while no abnormality was demonstrated in 6 patients. In the case of the cardioesophageal laceration, a defect was noted in the area, although a laceration was not specifically diagnosed until operation.

Forty-two patients who had definite gastric or duodenal lesions confirmed at surgical exploration had received preoperative x-ray examinations. In 31 (73.8%) of these barium studies, the gastric or duodenal abnormality seen by x-ray was present at surgery.

Surgical Procedures.—Of the entire group of 64 patients, 56 (87.5%) were treated by subtotal gastric resection. An additional two (3.1%) had total gastric resection, in one case for multiple gastric ulcers, and in the other for a large bleeding carcinoma near the gastric cardia. Thus, a total of 58 patients (90.6%) underwent gastric resection of some type as a definitive procedure. The remaining six patients (9.4%) were treated as listed below:

1. Ligation of bleeding gastric ulcer—patient's condition too critical to permit more extensive surgery.

2. Suture of stomal ulcer—this man had undergone subtotal gastric resection five weeks earlier at another hospital.

3. Exploration and pyloroplasty—no bleeding point found; recovery uncomplicated.

4. Suture and packing of ulcer—bleeding carcinomatous ulcer near cardia; no resection possible.

5. Exploration only—no site of bleeding was found and no definite procedure was done at this time.

6. Suture of laceration at the gastric cardia associated with repeated vomiting (Mallory-Weiss syndrome)—resection not considered necessary and the patient recovered satisfactorily.

All of the 56 definitive subtotal resections were of the Billroth II type; 40 (71.4%) were retrocolic and 16 (28.6%) antecolic. The two total gastric resections were completed by esophagojejunostomy and an accompanying jejunojejunostomy.

Mortality.—Over-all mortality for the series was 9 deaths (14.1%) in the 64 patients. Thirty-three patients were below the age of 50, and in this group there were two deaths (6.1%). In the 31 patients above the age of 50 there were 7 deaths (22.6%).

More detailed information on the patients who died is given in Table 10.

Complications Associated with Death.—It is readily seen that continued or recurrent bleeding was the commonest factor contributing to mortality and was associated with eight of the nine deaths. Sepsis of one type or another was the second commonest complication of lethal import and was present in five of the nine fatal cases.

Other Complications.—One or more complications were reported in 31 (48.4%) of the patients and are listed in Table 11. In 33 patients (51.6%) no complications were recorded.

Operative Surgeons.—Staff members performed 23 (35.9%) of the operations, with

TABLE 10.—*Data on Nine Fatal Cases*

Case No.	Age	Bleeding Site	Operation Performed	Factors Contributing to Death
1	74	Undetermined	Subtotal gastric resection	Continued bleeding, peritonitis, pneumonia; died 8 days postop.
2	58	Gastric ulcer	Subtotal gastric resection	Hypertensive cardiovascular disease, peritonitis, evisceration; died 16 days postop.
3	60	Duodenal ulcer	Subtotal gastric resection	Recurrent bleeding, peritonitis; died 30 days postop.
4	57	Duodenal ulcer	Subtotal gastric resection	Continued bleeding, cirrhosis of liver, severe; died 5 days postop.
5	17	Duodenal ulcer	Subtotal gastric resection	Continued bleeding, pyelonephritis, severe; died 36 hr. postop.
6	55	Gastric ulcer	Subtotal gastric resection	Continued bleeding, cirrhosis of liver, severe; died 36 hr. postop.
7	56	Duodenal ulcer	Subtotal gastric resection	Recurrent bleeding, died 11 days postop.
8	59	Gastric ulcer (carcinomatous)	Suture of gastric ulcer	Septicemia, peritonitis, continued bleeding; died 5 days postop.
9	36	Undetermined	Subtotal gastric resection	Continued bleeding, peritonitis, septicemia; died 29 hr. after second operation

4 deaths, for a mortality rate of 17.4%. Surgical residents, principally of the fourth-year level, performed the remaining 41 (64.1%) with 5 deaths, for a mortality rate of 12.2%.

TABLE 11.—*Nonfatal Complications*

Complication	No. Reported
Wound infection	12
Postoperative bleeding	10
Peritonitis	5
Psychosis (all transient)	4
Thrombophlebitis	3
Reoperation for continued bleeding	3
Pneumonia	2
Evisceration	2
Pulmonary infarction	1
Atelectasis	1
Empyema	1
Duodenal fistula	1
Cardiac decompensation	1
Reoperation for removal of foreign body	1

Comment

The method employed in the management of gastrointestinal hemorrhage will of necessity vary in different hospitals. At Brooke Army Hospital the Medical and Surgical Services have enjoyed several advantages favoring a combined approach to the problem.

1. Near proximity of the two services in the physical plant of the hospital, with prompt and, of course, free consultations between services

2. Laboratory, blood bank, and x-ray service available on a 24-hour-a-day basis

3. An emergency-ward arrangement, staffed and equipped to provide the continuous observation these patients require

4. A cooperative spirit at both staff and resident levels

The policy of vigorous replacement therapy in the resuscitative phase of management is advocated to restore a more normal blood volume and permit the early diagnostic efforts of esophagoscopy, gastroscopy, and upper gastrointestinal x-ray examinations. While such studies do not always determine the site of bleeding, they have frequently been of value, as indicated by the data in Tables 8 and 9.

No absolute criteria for surgical intervention are submitted. Both the Medical and the Surgical Services prefer to use a nonoperative regimen if blood replacement is effective in stabilizing the patient's vital signs, hematocrit, and hemoglobin. If such stabilization does not occur and the early endoscopy has ruled out esophageal varices as the bleeding site, surgical intervention is recommended to the patient, even if no definite gastric or duodenal lesion has been diagnosed by x-ray examinations.

Of the 10 patients in this series who had no definite bleeding point found at surgery, 8 had subtotal gastric resections, 1 underwent pyloroplasty, and 1 had exploration only. (The last patient bled again, and subtotal resection was done at another hospital, with recovery and no further bleeding at

follow-up, approximately four years later.) Two of these patients had recurrent bleeding after gastric resection and died. The remaining eight patients survived. Recently subdiaphragmatic vagus resection has been proposed as a definitive procedure in treatment of this group of patients, in preference to an empiric subtotal gastric resection.[10] Evaluation of the results of vagectomy is not yet possible.

While the over-all mortality rate of 14.1% is fairly acceptable, we should like to improve the results, especially in the over-50 age group. It will be noted from Table 10 that a surgical approach in Cases 1, 4, 6, and 8 was heroic in type and probably foredoomed to failure. Cases 2 and 5 had severe associated disease but were possible of salvage. Deaths in Cases 3 and 7 must be attributed to technical error, while the bleeding site in Case 9 was never identified and attempt at control by subtotal gastric resection was ineffective.

In Table 11 wound infections lead in the complication list. The combination of blood loss and contamination by the open gastric pouch certainly predisposes to sepsis. Usually antibiotics will control systemic manifestations but probably do not abort local wound infection. The problem of postoperative bleeding may be attributed to either technical error or the patient's disease, as previously discussed. Peritonitis of significant degree was present in five of the patients who died and undoubtedly contributed to the deaths. The transient psychoses were apparently associated with blood loss and possibly toxemia, although all of these patients recovered cerebral function. Pneumonia and evisceration were present in two patients who died. The remainder of the complications was not associated with death.

For the past six years General Surgery residents at the senior level have been permitted to assume operative responsibility for this difficult group of patients, and the results appear to justify the trust. In all instances staff surgeons were aware of the contemplated surgery and were available to provide assistance on request.

Summary

This paper concerns only those patients who underwent emergency surgery to control severe upper gastrointestinal bleeding. The following points are considered worthy of emphasis:

1. These patients benefit from a combined medical-surgical evaluation of their problem.

2. The results of the early diagnostic procedures of endoscopy and upper gastrointestinal x-rays appear to justify the effort required, without undue risk to the patients.

3. Blood transfusion requirements in these patients should be thought of in terms of one-half to several times the patient's estimated normal blood volume.

4. Although the mortality rate in the above-50 age group is more than triple that of the below-50 age group in this series, it is also true that the lives of 24 (77.4%) of the 31 patients above 50 were prolonged by surgical intervention.

5. Complications most frequently associated with death are those of continued or recurrent bleeding and sepsis.

6. Well-trained senior surgical residents may assume primary operative responsibility for these patients, with acceptable mortality rates.

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Transanastomotic Tube Feeding Following Gastric Surgery

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Not too infrequently there occur complications of gastroenterostomy which seriously interfere with the nutrition of patients in the postoperative period. The magnitude of the nutritional embarrassment is usually maximum irrespective of the severity of the complication, the degree of nutritional impairment relating only to the duration of the particular complication. With the advent of a simple and highly efficient method of tube feeding,[1] it seemed logical to apply this method to patients at the time of gastric anastomosis by guiding a fine polyethylene tube, indwelling in the stomach, through the stoma and into the efferent enteral loop at the time of performing open anastomosis. If it were found to possess no inherent disadvantages, such a tube could be left in situ until it was evident that no complications ensued and ingestion was feasible. Should, for any reason, ingestion be delayed, this already existent enterostomy could be employed. In long-term complications the enterostomy could be critical in recovery of the patient. In shorter-term complications the enterostomy could serve to maintain a better nutritional status than might otherwise be achieved, and to circumvent, in whole or in part, the ordeal of prolonged parenteral alimentation. This report concerns itself with the employment of these tubes, and with the use of continuous enteral feeding following gastroenterostomy.

Methods

Thirty-one patients had polethylene feeding tubes placed through a gastric anastomosis into the efferent enteral limb. In 16 the tube was used for feeding for varying periods of time. In 15 the tube was not used for feeding, and the tubes were removed when ingestion was established.

Four- and one-half-foot lengths of No. 15 polyethylene tubing were used. The tubing was connected to the rubber tubing of the drip apparatus by inserting the shaft of a No. 15-gauge hypodermic needle into the lumen of the polyethylene tubing and joining the hub of the needle to a glass connector tip.

When suture of the posterior layers of the gastroenteral anastomosis was completed, the polyethylene tube was recovered from the interior of the stomach, a foot of it drawn through the open stoma and threaded distally into the efferent enteral loop. The polyethylene tube traversed one of three pathways. In gastric resection with Billroth I or II reconstructions, the tube traversed the nares (Figs. 1 and 2). In most cases of simple gastrojejunostomy accom-

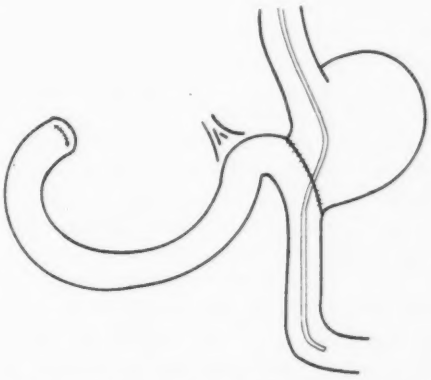

Fig. 1.—Nasogastrojejunal placement of tube used in gastric resection with Billroth II reconstruction.

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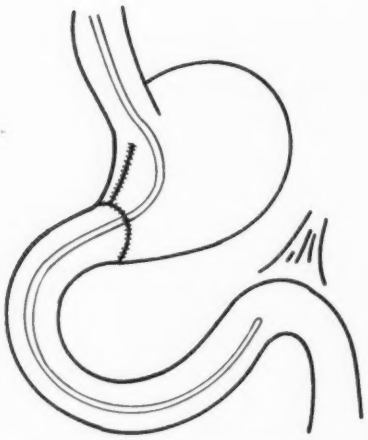

Fig. 2.—Nasogastroduodenal placement of tube used in gastric resection with Billroth I reconstruction.

panying vagotomy, a gastrostomy was created, using a Foley catheter. In these instances the polyethylene tube was placed through the catheter so as to be gastrojejunal in position (Fig. 3).

The polyethylene tube was brought to the stoma, prior to its recovery and passage into the efferent enteral loop, by one of three means. The commonest of these was to pass the tube through the nasopharynx and have it swallowed into the stomach on the day before the operation. This was always satisfactory when gastric resection was performed, as in this instance a large opening is made in the stomach through which search for the fine polyethylene tube is quite easy. Another method employed consisted of tying the distal tip of the polyethylene tube alongside the distal tip of the Levin tube, which was passed just prior to operation, and cutting the small tube free when the Levin tube was momentarily exteriorized through the stoma. When difficulty with these methods was encountered, or when it was decided at the time of anastomosis to use the long feeding tube, the proximal end of the polyethylene tube was tied to the distal end of the Levin tube, which was then withdrawn. The Levin tube was then cut free from the polyethylene tube outside the nares and repassed under anesthesia.

Feeding was not begun until ileus had subsided, as judged by at least auscultatory evidence. A proprietary feeding mixture,* suspended in water, was the feeding mixture used in all cases. The usual precautions in handling the reconstituted feeding mixture were taken.[1] Feedings were begun in a concentration of half that usually recommended (450 gm. added to 2 liters of water, yielding 1755 Cal.) and increased over a period of two to three days, or in accord with the patient's tolerance, to full concentration (900 gm. added to 2 liters of water, yielding 3510 Cal.). At the outset of feeding, the solution was given by continuous drip at a completely even rate of 50 ml. per hour and gradually increased, corresponding to the gradual increase in concentration, to 100 ml. per hour. Periodic aspirations of an indwelling Levin (or Foley gastrostomy) tube were made to determine the presence of a gastric, or a gastric pouch, residual. Only that amount of feeding mixture was placed in the infusion flask which would require one to three hours for deliv-

* Sustagen, which was supplied by Mead Johnson & Company, is a powdered food made from whole milk powder, nonfat milk solids, calcium caseinate, Dextri-Maltose, and dextrose, plus vitamins and minerals.

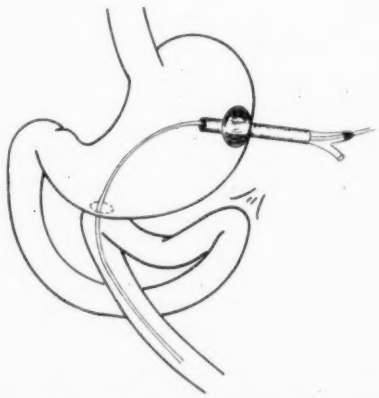

Fig. 3.—Gastrojejunal route used in vagotomy and gastroenterostomy.

ery, and every three hours the flask was rinsed and the connecting tube flushed with tap water.

Data

No complications could be ascribed to the use of the long feeding tube. There was no diarrhea as the result of feeding, and patients experienced nothing unfavorable from its employment. The tubes were quite easily placed and easy to care for, and in no sense imposed a burden upon those caring for the patient. Regurgitation of the feeding into the stomach or gastric pouch occasionally occurred, but when it did, was very small in amount. Feeding was instituted in 16 of the 31 patients, the tube being removed when the possibility of complications was apparently past and ingestion was successfully established. In the latter cases the tube was in place for an average time of 6.7 days, the range being 3 to 13 days.

In the 16 patients who were fed via the tube, the range of feeding was 2 to 22 days. Whether used for a short or a long period of time, in practically all instances the feeding replaced the need for parenteral alimentation after the first day. Some type of complication occurred in four cases of this group, and in these cases the durations of feeding were 7, 18, 18, and 22 days. In one of these patients, for safety, the tube was kept in place for 40 days. In this patient a valuable, and unexpected, diagnostic use was made of the long feeding tube.

Following are representative case reports of feeding in complicated cases; the last case includes a description of the diagnostic use to which the tube was put.

Case 1.—A 40-year-old man with a 15-year history of duodenal ulcer, which had become intractable, had been subject to frequent hemorrhages in the recent past. The 12-hour interdigestive secretion contained 73 mEq. of HCl. Vagotomy and posterior antrojejunostomy were performed. A gastrojejunal feeding tube was placed through a Foley gastrostomy catheter. The patient did very well during his initial postoperative course. Audible peristalsis appeared on the third day, and feedings through a long gastrojejunal feeding tube were begun on the fourth postoperative day. Continuing gastric balance tests showed a persistent gastric residual. On the 10th postoperative day barium visualization revealed delayed emptying without evidence of discrete obstruction. Throughout this time the patient had been fed via the long tube. Subsequent to the barium study, continuous gastric suction was maintained for four days, while feeding still progressed. At the end of this period the patient was given frequent small oral feedings until, on the 20th day, barium visualization revealed adequate emptying. Both gastrostomy and feeding tubes were removed at this time. The patient's weight at this time was 138 lb., which was the same as his preoperative weight.

Case 2.—A 68-year-old man had a history of weight loss, intractable epigastric pain, and roentgenographic evidence of gastric carcinoma. Gastric resection was performed, and a nasogastrojejunal feeding tube was placed. The early postoperative course was benign. Beginning on the fourth postoperative day, the patient presented a slowly dropping hematocrit, progressive ileus, and evidence of deep wound dehiscence. The patient was explored on the sixth postoperative day, and a slowly bleeding rent in the capsule of the spleen posterior to the gastrolienal ligament was found. Splenectomy was performed. Following surgery the patient developed a pneumonitis, with bilateral pleural effusion and a pneumothorax. His appetite was quite poor, and ingestion of any liquid precipitated nausea, although gastric emptying was adequate. For these reasons feeding via the long tube was instituted. The patient was fed for 22 days, until he regained his strength and, finally, his appetite. During the period of feeding, the serum albumin concentration rose from 2.5 to 3.2 gm. %.

Case 3.—A 65-year-old man with a known duodenal ulcer entered during a second episode of severe upper gastrointestinal hemorrhage. Gastric resection was done for hemostasis; at the time of the procedure no active bleeding was encountered. A nasogastrojejunal feeding tube was placed. During the early postoperative course the patient became edematous. Serum albumin was 1.9 gm. %. Venous pressure, circulation time, and heart size were normal. Even though the patient had arteriosclerotic heart disease and was maintained on digitalis, the medical consultants did not believe the patient was in congestive failure but attributed the edema to hypoproteinemia. On the fifth postoperative day feedings were begun through the indwelling long tube. He was fed for 18 days, during which time the edema disappeared and the serum albumin rose from 1.9 to 2.8 gm. %. Subsequent to this the patient convalesced rapidly and at the time of this report, six months later, is quite well.

Case 4.—This 78-year-old woman was admitted with marked chronic blood loss and a history of hematemesis, melena, and progressive weight loss

Fig. 4.—Barium swallow in Case 4 on the 10th postoperative day. The afferent, but not the efferent, loop is visualized after five hours.

during the previous six months. Barium visualization revealed a filling defect of the antrum, interpreted as carcinoma. At operation the tumor was found to have extended beyond the limits compatible with therapeutic resection, and so, because of bleeding and a 60% four-hour retention, palliative resection was carried out. Feeding was begun through a nasogastrojejunal tube on the third postoperative day. By the 10th postoperative day gastric balances were still positive, and so barium visualization was attempted. The afferent loop readily filled, but no barium had entered the efferent loop after a long period of time (Fig. 4). The barium was aspirated and the stomach irrigated, and on the following day a flat film showed no residual barium. At this time a thin solution of barium was injected into the feeding tube, and, with the patient in the Trendelenburg position, the barium was seen to flow readily into the gastric pouch via the efferent limb (Fig. 5). It was thus established that the obstruction of the efferent stoma was physiological, and not anatomical, in origin. On the following day the patient vomited the feeding tube. With the knowledge that the efferent stomal obstruction was physiological, she was placed on a dry diet for four days, after which her ingestive habits returned to normal.

Comment

Nasogastroenteral feeding was described in 1916 by Jones,[2] who used the Einhorn duodenal tube for feeding duodenal ulcer patients. Abbott and Rawson,[3] in 1939, introduced a double-lumen Einhorn-type tube, one lumen of which ended at the gastric level, the other lumen, designed for enteral feeding, continuing on to the metal bucket, which was allowed to descend into the duodenum. The seriousness of the nutritional problem in postoperatively complicated gastroenterostomy was recognized by Allen and Welch[4] in 1941, when they recom-

Fig. 5. — Barium injected into the nasogastrojejunal feeding tube on the 11th postoperative day (following evacuation of the gastric remnant). The gastric pouch readily filled via the efferent loop.

mended that routine, concomitant feeding jejunostomy be made in conjunction with gastric operations on underïourished patients. In 1942 Bisgard [5] advocated the use of two Levin tubes instead of the double-lumen Einhorn tube introduced by Abbott and Rawson.

No experience with patients was detailed in any of these publications, and none of the methods described seem to be in vogue today. This is not surprising, since the prolonged use of a Levin or an Einhorn tube for oro- or nasoenteral feeding is most impractical and fraught with complications. The method of using the fine polyethylene tubing described here is quite easy of application, completely tolerable to the patient, and without complications. Such nasogastric tubes have been left in situ for several months, for continuous or intermittent feeding, without any untoward sequelae or discomfiture to the patient.[1] Because of these facts, and because of the relative frequency and seriousness of nutritional problems immediately following gastric surgery, routine use of the method described here would seem warranted.

Enteral feeding has always been fraught with the danger of diarrhea. The diarrhea that accompanies this type of alimentation seems to stem primarily from the use of materials not iso-osmotic with body fluids and from an intolerance of the small intestine to fat. Homogenized milk plus an emulsifying agent was at one time recommended for enteral feeding.[6] The substance used in these studies possesses an osmolarity close to milk and is low in fat content (30

gm. per 900 gm. of the dry powder). The physical state of the milk protein is such as to produce very little gastrointestinal irritation. In a previous study of 6974 days of nasogastric tube feeding in 240 patients using this feeding mixture,* very minimal diarrhea was encountered.[1] The feeding material can be used in such concentrations as to provide a high caloric diet. It is high in protein and carbohydrate and low in fat and sodium. Vitamins and minerals are present in amounts recommended as therapeutic by the Committee on Therapeutic Nutrition of the National Research Council.[7] Previous studies have demonstrated the metabolic efficiency of the mixture.[1,8]

If feeding complications are to be avoided, it is necessary to bear in mind that the material used is a fermentable substance. After suspension of the powder, the material must be refrigerated, as is milk, and aliquots should not be exposed to room temperatures for more than short periods of time. Furthermore, the external delivery apparatus should be frequently rinsed with tap water. In these studies, only that amount of liquid diet was placed in the drip flask which would require one to two hours for administration, and the external apparatus, including infusion flask, was rinsed with tap water every three hours. In the cases reported, no diarrhea or other complications of feeding were encountered.

Summary

A small-bore polyethylene feeding tube was placed through the gastric stoma into the efferent enteral loop at operation in 31 patients. These tubes took a nasogastrojejunal, nasogastroduodenal, or gastrojejunal route.

Of the 31 patients, 16 were fed through these tubes postoperatively, obviating the necessity of parenteral alimentation.

In four complicated cases, feeding was prolonged and vital to the nutritional maintenance of the patients.

No untoward reaction occurred from the use of these tubes or from continuous alimentation through them.

The use of small-bore polyethylene feeding tubes through gastric anastomoses is recommended as a routine prophylactic measure.

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Editorial

Postoperative Mortality

A Major Consideration in Selection of an Operation for Duodenal Ulcer

In a recent survey [1] made by a committee of the Ohio Chapter of the American College of Surgeons, with Dr. S. O. Hoerr as chairman, it was found that for the group of 29 hospitals regarded as being among the best in the State of Ohio the mortality for a total of 2562 elective operations for duodenal ulcer was 4.3%. Eighty-nine per cent of the operations were performed by Board-Certified surgeons or Fellows of the American College of Surgeons. This mortality occurred in the past five years and did not include deaths following emergency operations for bleeding or perforation. The highest reported mortality was 7.8% and the lowest 0%.

Differences in mortality appeared to be mainly the result of differences in the types of operation employed. The state-wide mortality for elective gastric resection was 4.9%, whereas the mortality for operations exclusive of resection (mostly vagotomy with a drainage procedure) was 1.7%. In general, the highest mortality occurred in those hospitals in which resection was the standard treatment, and the lowest mortality occurred in those hospitals in which a high proportion of the patients were treated by vagotomy combined with gastroenterostomy or pyloroplasty.

Duodenal ulcer, unless bleeding or perforated, is rarely fatal. Its presence, although a source of discomfort and inconvenience, is not incompatible with long and useful life. Since it is better to be alive with a troublesome ulcer than to be cured of it at too great risk, the mortality of operations for duodenal ulcer is a consideration of paramount importance.

If we take the Ohio committee's 4.9% as the average mortality following gastric resections done by surgeons who employ gastric resection as the sole treatment of duodenal ulcer, 49 of 1000 patients operated on might die after operation. If pyloroplasty or gastroenterostomy were the sole procedure employed, the average death rate might be 1.7% and 17 patients might die. But the curative effects of the two operations are quite different. If vagotomy is added to gastric resection, or if a radical subtotal gastrectomy is performed, the recurrence rate approaches zero. On the other hand, within from 5 to 10 years, approximately 5% of the patients treated by vagotomy with either pyloroplasty or gastroenterostomy will require gastric resections to control recurrences. Fifty of an original one thousand patients will have to be operated on again and will incur the 5% risk of gastric resection. Two or three of them may therefore die following secondary procedures.

If the mortality of patients subjected to gastric resection is compared with the ultimate surgical mortality of those treated by vagotomy with drainage opera-

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tions, it is apparent that the conservative operations are in the long run the safer (Table).

Operative Mortality

Gastric Resection (With or Without Vagotomy)		Vagotomy with Gastroenterostomy or Pyloroplasty	
Cases	Deaths	Cases	Deaths
1000	49	1000	17 (immediate) 2 (following secondary operations)
	Total		19

The difference between these two death rates is striking. The same general relationship applies to the risk of gastric resection as compared with that of vagotomy with drainage operations, even in the hands of surgeons of the highest skill and with the greatest experience. Regardless of their ability, few surgeons could employ gastric resection in every patient undergoing elective operation for duodenal ulcer without incurring a mortality of 2%. However, surgeons of comparable skill, if experienced in the method, could perform vagotomy with gastroenterostomy or pyloroplasty on every patient with a mortality of 0.5%.

There is no question that a radical subtotal gastrectomy or a hemigastrectomy and vagotomy gives better control of the ulcer diathesis than does vagotomy with lesser operations. But the prolonged or permanent incapacities that some patients incur following resections, and the increased mortality that attends these operations, vastly outweigh the disadvantages of the recurrences that follow more conservative procedures. Moreover, the recurrences after conservative operations are correctible, and sooner or later all patients can be relieved of their symptoms of ulcer.

In the treatment of duodenal ulcer the survival of the patient is the most important consideration. The Ohio survey should be studied seriously by all who are interested in the elective surgical treatment of duodenal ulcer.

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Diagnostic Paracentesis

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The value and safety of simple needle tap of the abdominal cavity has long been recognized as an aid in the differential diagnosis of the acute abdomen. Despite its value, the procedure has failed to gain general acceptance. This lack of acceptance may be based upon an unjustified fear of puncturing the bowel, or it may be due to the unreliability of former techniques.

A survey of the literature combined with our experience in more than 100 cases has served to dispel concern over the rare occurrence of entering the bowel lumen.

Diagnostic paracentesis should be considered only as another test to aid in the construction of a more definite, clear-cut clinical picture. This is especially evident in the differential diagnosis of complex or unusual problems associated with intraperitoneal disease or traumatic injury. In many instances the results of a tap are conclusively self-explanatory and the clinical problem is at once solved. However, the results of all paracenteses may have the appearance of too high a percentage of inaccuracy unless, as in any other test or laboratory procedure, the information is properly integrated and evaluated. We do not recommend empirical reliance upon this single test. As in any other test, experience increases its value, and we recommend its routine use in any acute abdominal situation in which the diagnosis is not clearly established by other diagnostic means.

As early as 1906 a very similar technique was described by Salomon.[20] His method involved passing a ureteral catheter through a needle within a trochar to obtain diagnostic aspirate. A variety of needles have been employed. These include capillary glass tubing,[4,9] spinal needle,[5] and a Potter needle [22] which includes a stylette.

Special methods of study of the aspirated fluid [21] suggest that quantitative studies of bacteria and phagocytic activity provide prognostic value, as well as diagnostic aid. Many authors [1-3,16,18] have pointed out that a grossly negative tap may produce the essentially diagnostic information from one drop of peritoneal fluid which has been caught in the needle barrel or syringe tip. Frink [6] feels that 200 cc. is the minimum quantity of intraperitoneal fluid likely to yield a positive tap, and he suggests the injection of saline to increase the likelihood of fluid return.

A negative tap is generally held to lack clinical significance [5,7,25]; yet Anderson [1] suggests that increased experience will improve reliance upon negative results. Two negative taps [14] argue against operation. This is especially pointed out by Thompson,[22] who has stated that of 300 diagnostic taps he knows of no case in which a negative tap was obtained and major abdominal pathology was later revealed. Villafane [26] advises diagnostic puncture in the false-acute abdomen as an aid in avoiding operation. Moretz and Erickson,[15] however, found fluid present at operation in seven cases when the peritoneal tap was negative.

Unnecessary operations can be eliminated by the detection of primary Pneumococcus, Staphalococcus, or Gonococcus,[1-3,5,10] by the identification of acute pancreatitis,[1,12,14,16,25] and by the differentiation of appendiceal and primary peritonitis, as suggested by Salomon,[20] Horsley,[10] and Touroff.[23]

Keith [12] has found much higher amylase levels in the peritoneal fluid than in serum. In fact, he stresses the importance of peritoneal fluid amylase levels late in acute pan-

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creatitis, for such an analysis the diagnosis may often still be established after the serum level has fallen to normal. Thompson [22] has added a collection of three cases of acute hemorrhagic pancreatitis with normal serum but with elevated peritoneal fluid amylase.

Pfeffer [18] has found peritoneal fluid amylase levels of from 7800 to 19,600 mg. % in the four cases of hemorrhagic pancreatitis.

In experimental strangulation in dogs, Hill [8] found that the typical fluid of strangulation described by Scott and Wangensteen [19] had developed within four hours. Wangensteen [27] has described the fluid of simple obstruction as clear and straw-colored.

Kaufman [11] has successfully employed peritoneal tap after giving methylene blue by mouth to identify a perforated peptic ulcer. Multiple quadrant taps of the abdominal cavity have been utilized by Touroff [23] to determine the degree and spread of peritonitis. The detection of internal bleeding in an unconscious patient is reported by Henry and Vale [7] and by Thompson and Brown.[22]

There is general agreement upon the safety of abdominal tap.[1-3,5,7,11,14,16,17,21-23,28] No serious complications have been described. Although few contraindications have been listed, bowel fixation by adhesions or an inflammatory process [1,16,21,23] and marked bowel distention [21] are suggested as valid objections to its use. If, because of fixation to the abdominal wall, the bowel is entered by the needle, no harm need be anticipated.[2,11,17] Campbell [2] and Thompson [22] point out that the finding of a multiplicity of organisms and absence of pus cells on smear of the peritoneal aspirate indicates that the needle was in the bowel.

Observations in Personal Series

In the evaluation of intraperitoneal disease, the paracentesis is of outstanding value. This series includes a study of more than 100 abdominal taps by this method.

Trauma.—Of 12 patients in whom paracentesis was done for abdominal trauma, a bloody tap, confirmed by operation, was found in 11. The other patient recovered without operation. One patient with complex injury involving a ruptured spleen, pancreas, and duodenum might well have been saved if the tap and the operation had been done on the first instead of the third day after admission.

A patient with contused left kidney with bloody urine was also found to have a ruptured spleen. This situation might easily have been missed if an abdominal tap had not been done. In another instance of abdominal trauma a negative tap associated with left renal injury gave security in the decision not to explore the abdomen. Similarly, in a case of large retroperitoneal hematoma with reflex inhibitory ileus, a negative tap added security to the decision for conservative management.

Ruptured spleen without other associated problems appeared four times in this series. Aside from hastening and strengthening the decision to operation, the discovery of a fresh bloody abdominal tap may well have saved such a case of multiple body injuries as one which involved unconsciousness. This series also includes two cases of ruptured liver. Diagnosis was made at operation after free blood was found on paracentesis.

The presence of bloody urine in the abdomen establishes definite rupture of the urinary bladder. In one of two cases in this study, 150 cc. of bloody urine was obtained by urethral catheter, suggesting contusion rather than rupture. The presence of urine within the abdomen obviously established the diagnosis of ruptured bladder. It is our belief that in trauma in which abdominal injury is suspected from positive physical findings or in an unconscious injured patient, a diagnostic paracentesis should be as much a part of the clinical evaluation as catheterization, rectal examination, or x-ray.

Pelvic Pathology with Blood.—Diagnosis of intra-abdominal bleeding from ruptured ovarian cyst (three cases) and from bleeding ectopic pregnancy (three cases) is aided by diagnostic tap. In two cases the diagnosis of ectopic pregnancy was not established on the basis of the peritoneal tap. On the other

hand, the presence of blood in the peritoneal tap confirmed the diagnosis in a case made difficult by known previous episodes of salpingitis.

Pancreatitis.—The chemical irritation of acute pancreatitis produces an acute abdomen which often cannot be differentiated from an acute surgical abdomen; yet the former condition is usually better treated nonoperatively. The presence of clear yellowish to brown fluid with a positive test for trypsin yields a rapid differential from the bile of perforated gallbladder, the cloudy fluid of perforated peptic ulcer, or the pus and Escherichia coli organisms of a ruptured diverticulum or appendix. In one very unusual situation in this series the tap produced both bile and pancreatic juice, owing to hemorrhagic pancreatitis and a slough or rupture of the common bile duct.

Peptic Ulcer.—The fluid obtained in perforated peptic ulcer is cloudy, due to debris, mucin, and some pus reaction. A smear frequently yields yeast cells and may have a wide variety, but lack of abundance, of bacteria. In two of five cases air was presented in the tubing and syringe.

Inflammatory Processes.—Inflammatory conditions of infectious origin produce varying quantities of pus. A direct smear using the Gram stain gives considerable assistance to diagnosis. A diagnostic paracentesis which yields pus is much less specific than blood, bile, or pancreatic or gastric juice. However, in a few cases pus of a specific type on the smear assisted in avoidance of operation. On one occasion an acute abdomen developed two weeks after a diagnostic D and C; the abdominal tap fluid produced a smear similar to one taken from the cervix. In another case the identification of pneumococci permitted successful nonoperative treatment.

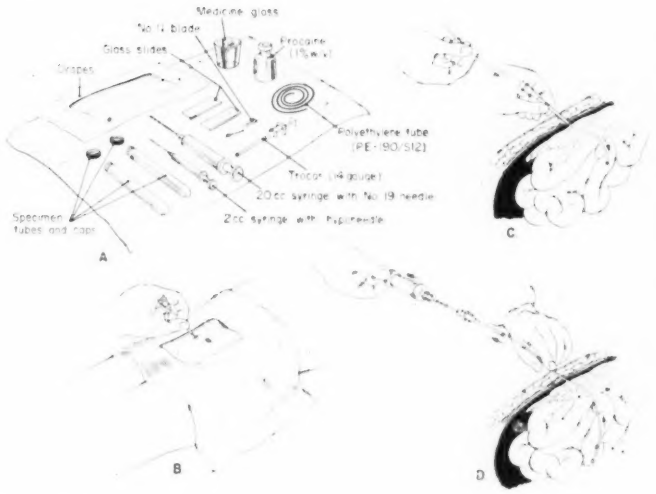
In pelvic inflammatory disease the differentiation of abscess, chronic pyosalpinx, or more diffuse pelvic peritonitis seemed to be dependent upon physical examination and other laboratory findings more than on the diagnostic tap. In eight cases of pelvic inflammatory disease in which operation was performed, at least four could have been managed on antibiotics alone. The greatest aid in pelvic disease would appear to be in eliminating the presence of blood.

Biliary Disease.—The acutely inflamed gallbladder produces varying degrees of inflammatory, infectious, or exudative peritoneal response. Of 10 cases, none was misleading, but 2 cases produced valuable information which warranted immediate surgery. One of these revealed free pus in the peritoneal cavity, and the other revealed bile.

Intraperitoneal Vascular Disease.—In the intra-abdominal vascular accidents of mesenteric embolism, thrombosis, or strangulation obstruction ascitic fluid of clear, brownish color rapidly developed. Very early after the onset of vascular accident a tap producing clear yellow fluid may be misleading, and, therefore, time must be given some consideration. In one of three cases of mesenteric vascular occlusions, the tap was in error, due to failure to obtain fluid. In three strangulation obstructions, the brownish or wine-colored paracentesis fluid lent support to the sense of urgency in therapy.

False-Acute Abdomen.—In the false-acute abdomen obviously a negative tap is obtained. As experience is gained in the procedure, one is able to sustain greater reliance upon negative findings. A small volume of clear fluid was obtained in one case of infectious mononucleosis. A more impressive example of security from negative findings developed in the case of a 10-year-old boy who presented a board-like abdomen and was found to be in severe diabetic acidosis. A completely negative paracentesis eliminated the possibility of ruptured appendix or other peritonitis as antecedent to or initiating the diabetic imbalance.

These examples will no doubt expand, and experience may be expected to reveal even more diverse points of assistance to the surgical clinician.



A, set-up of equipment for diagnostic paracentesis; *B*, site of tap; *C*, insertion of polyethylene tube; *D*, withdrawal of diagnostic fluid.

Technique of Diagnostic Paracentesis

A variety of techniques have been described.[2,11,13,15,16,24]

The technique which we have been using for the past five years is very similar to that which was described by Pfeffer.[18] Some points which have been found to be of value are pointed out in the following procedure:

1. Sterile prep and draping is carried out in the patient's bed.

2. Procaine infiltration of the skin, fascia, and peritoneum is done 1 in. lateral to the midline and below the umbilicus.

3. A 2 mm. incision is made in the skin to keep the needle from binding.

4. A 4 in. styletted needle, 14 gauge, is used. The resistance of both the posterior and the anterior rectus sheath is identified as the needle passes through. The styletted needle prevents plugging by fat or other tissue and picking up of blood as the needle passes through the abdominal wall.

5. After the needle has entered the peritoneal cavity, 12 to 18 cm. of polyethylene tube is threaded through the needle and into the peritoneal cavity. (It may be advisable to wait a minute or two, as suggested by Hill[8] in order to allow fluid to enter the polyethylene tube.)

6. The needle is then removed and the polyethylene tube is left in. One should never remove the polyethylene tube through the intact needle, as a double or bent tube may be sliced off.

7. Air or saline, 2 or 3 cc., is injected to determine the absence of a kink in the polyethylene tube.

8. Gentle aspiration with a syringe is used as the polyethylene tube is slowly withdrawn. The patient's position may be changed during this procedure.

One must not misinterpret a small spurt of blood as the polyethylene tube is pulled back out through the last 2 in., as this may come from the perforation of the abdominal wall. If precautions have been taken to be certain of entering the peritoneal cavity, bleeding from organs within the peritoneal cavity usually appear early in the aspiration. Clotted blood from the abdominal wall will appear near the end of withdrawing the polyethylene tube.

A positive tap is obviously more significant than a negative tap, but with practice one learns to depend upon the negative results. Our impression agrees with others in that perforation is more likely to occur where bowel is adherent to the abdominal wall and, therefore, scarred area of the abdominal wall should be avoided.

We have had the experience of cutting off a tube in the peritoneal cavity, having been careless in removing the tube while the needle was still in the abdominal wall. In two instances the bowel was perforated, as evidenced by smears which contained multiple bacteria and/or obvious small-bowel content. No complications or sequelae developed in either case.

Summary

A technique of refinement in diagnostic paracentesis is presented. The insertion of a long tube of polyethylene is suggested as a means of increasing the reliability of this peritoneal tap.

We have found the method infinitely satisfactory in aiding in the diagnosis of otherwise difficult problems, and in many instances it has been the diagnostic aid that has definitely established the subsequent correct treatment in the acute, as well as the pseudoacute, surgical abdomen.

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Cardiac Reflexes in Pulmonary Embolism

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The cause of death from a small pulmonary embolism is not clearly understood. There is reason to believe that deleterious cardiac reflexes may occur, but their appearance has not been verified experimentally.[1-3] However, the investigators cited have used heart-lung preparations or anesthetized animals in which reflexes would probably be abolished, and their results, therefore, are of questionable value. It is obvious that a method must be used whereby these studies can be performed on unanesthetized animals.

This laboratory has previously studied pulmonary vasoconstriction associated with pulmonary embolism in unanesthetized rabbits, and we feel that a correlation of such studies with the electrocardiographic pattern may throw some light on the problem. We should also like to report on some preliminary hemodynamic studies concerning a possible terminal mechanism of death in pulmonary embolism.

Pulmonary Vasoconstriction

Our method of study has been the injection of a standard dose (1 cc/lb. of a 0.48% solution) of 5μ-sized graphite particles (Dixon's Airspun Micronized Graphite, Type 200-09) into animals and studying their distribution in the lungs. The average number of graphite-filled blood vessels (20μ in diameter or larger) per low-power field is used as an index of vasoconstriction. With vasoconstriction, the graphite particles collect in the arterioles, and the number of graphite-filled arterioles per low-power field is relatively high. In the absence of vasoconstriction the graphite particles diffuse into the capillaries, and the number of graphite-filled arterioles is low. In this manner the microscopic data can be presented in tabular form.

It has been found that anesthesia with ether and pentobarbital (Nembutal) abolishes vasoconstriction.[4] Vagectomy appeared to have no particular effect on

TABLE 1.—*Summary of Experimental Data on Pulmonary Vasoconstriction* Associated with Pulmonary Embolism in the Rabbit*

Drug	Dose	Rabbits, No.	Arterioles per Low-Power Field
A. Previous studies			
Control		17	20.5
Ether		12	6.3
Pentobarbital		15	3.3
Atropine	2.17 mg.	10	4.7
Vagectomy		11	14.7
Tetraethylammonium (Etamon)	30 mg/kg.	14	3.7
Tolazoline (Priscoline)	25 mg.	12	3.8
Epinephrine	0.01 mg/kg.†	8	4.0
	0.01 mg/kg.‡	8	1.5
	0.01 mg/kg.§	15	17.2
B. Present studies			
O_2 inhalation		10	9.7
O_2 positive pressure		10	10.2
Papaverine I. V.	15 mg.	10	10.5
Serotonin	0.05 mg/lb.†	10	33.2
	0.05 mg/lb.§	10	30.3
S U 3822 †	5 mg/kg.	12	1.0

* The degree of vasoconstriction is a direct function of the number of graphite-filled arterioles seen per constant low-power microscopic field.

† Intravenous, 10 minutes before embolism.

‡ Subcutaneous, simultaneously with embolism.

§ Intravenous, simultaneously with embolism.

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vasoconstriction, whereas atropine markedly eliminated it, probably by a direct effect on the blood vessel, and not by way of the vagus nerve.[5] Studies with various drugs affecting the sympathetic nervous system revealed that ganglion- and adrenergic-blocking agents eliminated the vasoconstriction. Epinephrine in small doses was found to produce a transient pulmonary vasoconstriction, yielding to a more prolonged vasodilatation[6] (Table 1A).

A study of the effect of additional agents on the pulmonary circulation of the unanesthetized rabbit has recently been completed. Oxygen and positive-pressure oxygen inhalation, papaverine, serotonin, and SU3822* were employed (Table 1B). It appears that oxygen inhalation and papaverine are mild vasodilators, whereas SU3822 is a strong vasodilator. Serotonin is a potent vasoconstrictor.

In summary, it would appear that a pulmonary vasoconstriction is associated with this type of experimental embolism in the rabbit which is not mediated through the vagus nerve. It is probably a local vascular response, although there may be some modifying effect of the sympathetic nervous system.

Cardiac Studies

It is felt that a correlation of these pulmonary vasoconstriction studies with the electrocardiographic pattern produced by pulmonary embolism might shed some light on the presence of cardiac reflexes.

During acute cor pulmonale, visualization of the heart reveals a dilatation of the right ventricle, pulmonary conus, and auricle associated with a decrease in the volume of the cavities on the left. This causes the left ventricle to be displaced upward and backward with a clockwise rotation.[7] An increase in right intraventricular pressure occurs, which may produce ischemia of the right side of the heart from a purely mechanical effect or from a disturbance of the coronary circulation. Several rhythm disturbances may be seen, such as auricular flutter and fibrillation, pulsus bigeminus, and AV blocks. The cause of death is usually ventricular fibrillation with occasional ventricular standstill and AV block.

The electrocardiographic disturbances which accompany these changes have been summarized by Karlen and Wolff,[8] using vector and ordinary electrocardiography.

The initials QRS vectors were directed superiorly and slightly to the right and usually were greater than normal in magnitude. Thus Q waves are seen in Leads II, III, and aV_F.

The terminal vectors were directed to the right posteriorly and superiorly and were of larger magnitude than normal. Thus S waves may be seen in Leads aV_L, I, II, and III with a late R wave in aV_R. These electrocardiographic results clarify markedly the previous pattern, which had been so well described by McGinn and White,[9] i. e., the S_1-Q_3 pattern. At the same time, a shift of the transitional zone to the left was found in the precordial leads. This was corroborated by other investigators.[10,11]

As evidence of right ventricular ischemia, the QRS-T vector angle is abnormal and the S-T-segment vectors are displaced to the right. Rhythm disturbances, such as auricular flutter and fibrillation and right bundle-branch block, have been found in human cases.

In the course of studies on pulmonary embolism in dogs, using a constant embolizing infusion of barium, a fairly characteristic hemodynamic pattern is found. The cardiac output falls, and the pulmonary artery pressure and pulmonary vascular resistance increase. Terminally, the cardiac output continues to fall and the resistance to rise, but the pulmonary artery pressure begins to drop as the right heart fails until the animal dies. The S-T-segment changes do not appear usually until the peak of the pulmonary artery pressure is approached (12 of 13 animals; Fig. 1).

*This drug [1-benzyl-2-(2-dimethylaminoethyl)-isoindoline dihydrochloride] was supplied through the courtesy of Ciba Pharmaceutical Products, Inc.

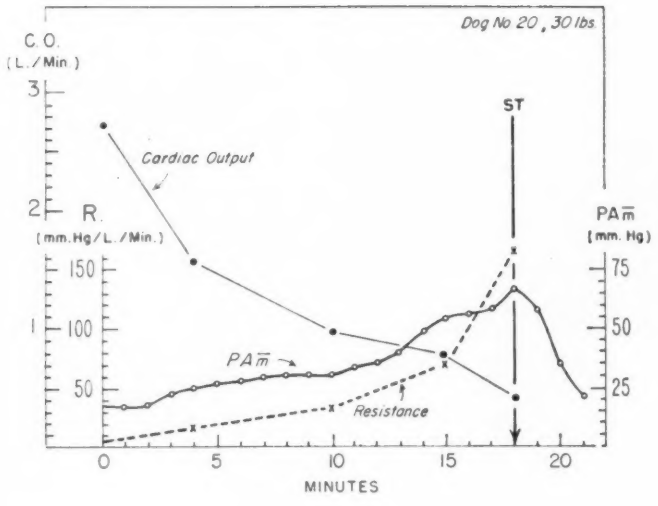

Fig. 1.—Typical hemodynamic pattern of experimental continuous pulmonary embolism, showing onset of S-T-segment changes with the peak of pulmonary artery pressure just prior to failure of the right heart.

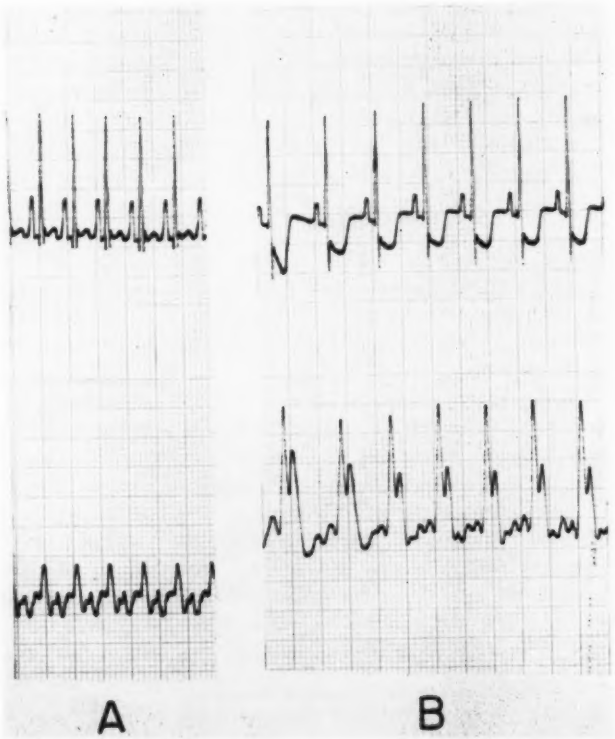

Fig. 2.—Relative tricuspid insufficiency with pulmonary embolism. *A*, tracing of vena cava pressure prior to embolism, showing normal pattern with typical x-descent with onset of ventricular systole. *B*, same tracing during terminal phases of pulmonary embolism, showing elevated venous pressure with a venous pattern of tricuspid insufficiency. The x-descent has been replaced by a peak corresponding with ventricular systole.

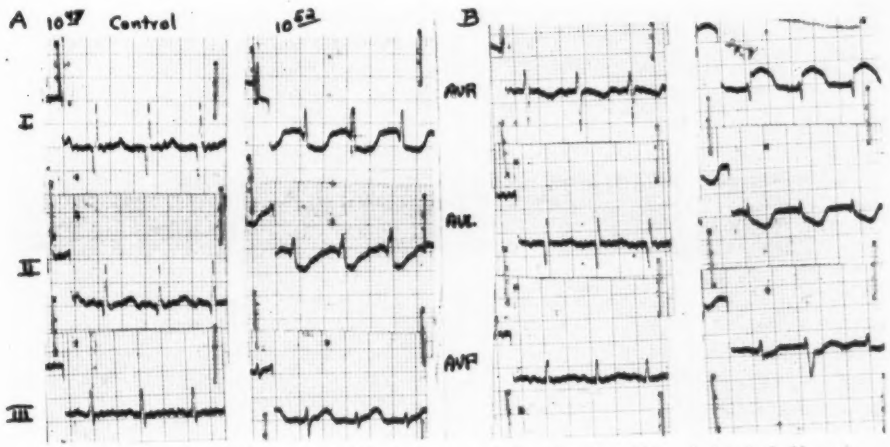

Fig. 3.—Standard EKG pattern of pulmonary embolism in the rabbit. *A*, Leads I, II, and III. Left tracings: control; right tracings: five minutes after severe pulmonary embolism. *B*, Leads aV_R, aV_L and aV_F; left and right tracings same as in *A*. Marked S-T-segment shift, with vector pointing to right.

The fall in pulmonary artery pressure may be due to something other than right ventricular failure. Preliminary studies on vena cava pressures reveal the onset of tricuspid insufficiency as the pulmonary arterial pressure increases (Fig. 2).

In order to establish the electrocardiographic pattern in the rabbit, a 1.5 cc. per pound dose of the previously mentioned graphite solution was injected, and it proved to give a fairly consistent electrocardiographic pattern which closely resembled the previously described human pattern and still had a low mortality rate in the experimental animal. The main QRS complex tended to become horizontal, and the terminal appendage was directed to the right and superiorly. S-T-segment changes and QRS-T-angle changes were distorted in the majority of animals (Fig. 3).

Once this standard pattern was established, the effects of all previously mentioned drugs were studied on the rabbit. Since the QRS complex in the rabbit is so brief (0.02-0.04 second), it was difficult to use it as a test point. However, since we have previously shown that S-T-segment changes have an ominous significance, and since they are so readily discernible on the electrocardiogram, it was decided to use them to gauge the effect of pulmonary embolism on the heart.

As can be seen (Table 2), agents that were associated with minimal or no vasoconstriction (ether, pentobarbital, atropine, tetraethylammonium chloride [Etamon], tolazoline [Priscoline], SU3822, or epinephrine, given 10 minutes prior to embolism or given in small doses simultaneously

TABLE 2.—*Summary of Experimental Data Demonstrating Effect of Various Drugs and Procedures on a Standard Pulmonary Embolism*

Drug	Rabbits, No.	ST-Changes	Mortality, %
Control	10	9	10
Ether	10	1	30
Pentobarbital	10	1	0
Atropine	10	0	0
Vagectomy	10	5	0
Tetraethylammonium (Etamon)	10	2	0
Tolazoline (Priscoline)	10	4	10
Epinephrine			
I.V. 10 min. prior to embolism	10	2	0
Sub. ent. simultaneously	10	1	10
I.V. simultaneously	10	7	40
O_2, inhalation	10	4	30
O_2, positive pressure	10	5	30
Papaverine	10	5	10
Serotonin			
I.V. 10 min. prior to embolism	10	4	0
I.V. simultaneously	10	7	10
SU3822	10	1	0

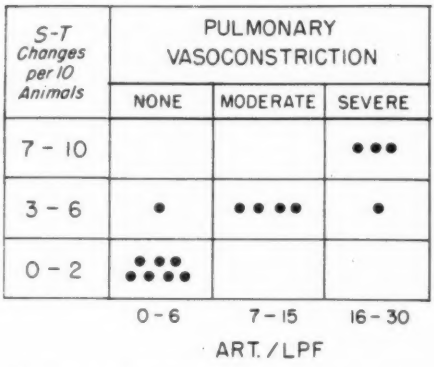

Fig. 4.—Correlation of pulmonary vasoconstriction with severity of cardiac changes.

with embolism) showed few cardiac changes, with one exception (tolazoline). However, those agents that were associated with severe vasoconstriction (control, vagectomy, epinephrine given intravenously and simultaneously with the embolism, and serotonin) showed the most cardiac changes. The rest of the drugs were intermediate in action. If the degree of vasoconstriction, as shown by the number of arterioles per low-power field, is correlated with the degree of S-T-segment changes, one will find what appears to be a significant correlation between the two (Fig. 4). In other words, agents associated with vasodilatation give few S-T-segment changes, whereas those associated with a high degree of vasoconstriction give severe S-T-segment changes.

Comment

Salvage of a patient from pulmonary embolism is a tug of war between the pulmonary resistance and the pumping action of the heart. With a constant pumping action, the size of the embolus or the degree of associated pulmonary vasoconstriction will decide the outcome. When the resistance remains constant, the reserve of the cardiac muscle is the all-important factor. Diseased hearts will thus succumb to smaller emboli than normal ones. The relative tricuspid insufficiency which we have demonstrated is another variable to consider. Certainly, when present, it will greatly decrease the ability of the right heart to pump blood through collateral pulmonary channels at a very critical time. It may represent the point of no return with pulmonary embolism!

Experimental studies are very confusing. There is great variation from species to species with regard to pulmonary vessel reactivity and the relation of heart strength and weight to total body weight. It is certainly apparent that rabbits demonstrate pulmonary vasoconstriction with embolism. These experiments with minute emboli demonstrate a close parallelism between pulmonary vasoconstriction and S-T-segment changes. Thus it would appear that ventricular ischemia producing the S-T-segment changes is due to increased intraventricular pressure secondary to the rise to pulmonary resistance and is not related to a reflex coronary spasm. This pulmonary vasoconstriction is not modified by vagectomy, but it can be relaxed with vasodilating adrenergic- and ganglion-blocking agents, as well as anesthesia.

Thus if any reflexes are present in the rabbit, they are local vascular ones in the lung, and not coronary artery reflexes.

Summary

Establishment of a correlation of the cardiac changes found in pulmonary embolism and various agents known to affect the pulmonary vascular resistance was undertaken in rabbits. It would appear that there is a close parallelism between the degree of pulmonary vasoconstriction and the severity of the cardiac changes. This correlation would seem to indicate that the cardiac changes are due to increased intraventricular pressure secondary to the pulmonary embolism and associated vasoconstriction, and are not related to a reflex coronary spasm.

Preliminary work on dogs reveals that a relative tricuspid insufficiency may play a role in reducing the pumping action of the heart at a critical phase of pulmonary embolism.

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Evaluation of the Fine-Particle Skin Autograft Technique

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Introduction

For many years surgeons have searched for a better method of securing coverage of large, full-thickness skin defects that result most commonly from thermal injury. The coverage of these large defects is time-consuming and difficult, often requiring multiple skin autografts. At times sufficient autograft donor sites are not available, and long intervals occur between grafting procedures, until the donor areas are healed and can be used a second time.

There is a real possibility that atomic weapons will be used in any future world conflict and cause large numbers of extensive third-degree burns that will require grafting.

Recently Najarian, Crane, and McCorkle [3] described a skin autograft technique using fine skin particles prepared in a food Blendor. These investigators reported that in using this technique they were able to cover 9 to 10 times the area that is covered by equal amounts of solid-sheet, split-thickness autografts.

The studies reported in the present paper were designed to evaluate the effectiveness of this fine-particle skin autograft technique. Our object was to determine (1) the extent of coverage that could be obtained, (2) the effect upon the amount of fluid loss from the defect, (3) the protection afforded against infection, and (4) the characteristics of the resulting scar as to the degree of contraction, fixation, and ability to tolerate trauma.

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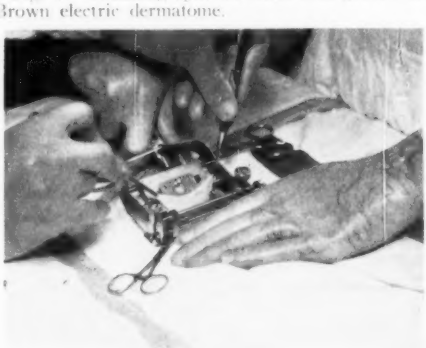
Work performed in the Laboratory, U. S. Army Surgical Research Unit, Brooke Army Medical Center, Fort Sam Houston, Texas.

Resident, General Surgery Service (Captain Cox); Chief, Department of Surgery (Colonel Nichol), Brooke Army Hospital, Brooke Army Medical Center, Fort Sam Houston, Texas.

Materials and Methods

Forty adult rabbits, each weighing between 9 and 14 lb., were used in the experiment. These rabbits were divided into 10 groups of 4 each. Four rabbits were operated upon at a time, and one of each group of four was used as a control. The animals were anesthetized by intramuscular paraldehyde or intravenous pentobarbital sodium, after which a 15×15 cm. area on the right dorsal trunk was shaved and prepared surgically with ether and 70% alcohol. The operative area was draped with surgical towels, and a 10×10 cm. split-thickness skin graft was removed, using a Brown electric dermatome set at 0.010 in. (Fig. 1). One-tenth of this graft, a square measuring 3.2×3.2 cm., was cut into small particles, using scissors, and then placed in a semi-micro-Blendor. The remaining nine-tenths of the skin graft was discarded. Twenty-six cubic centimeters of chilled isotonic saline was added as a diluent in the Blendor. Chilled saline was used to control temperature rise. The skin was minced in the Blendor for five minutes, transferred to a sterile test tube, and centrifuged for five minutes. The supernatant saline was poured off except for 2 to 3 cc. By agitating the tube, the remaining saline was mixed with the precipitate of skin particles.

Fig. 1.—Obtaining split-thickness skin graft with Brown electric dermatome.



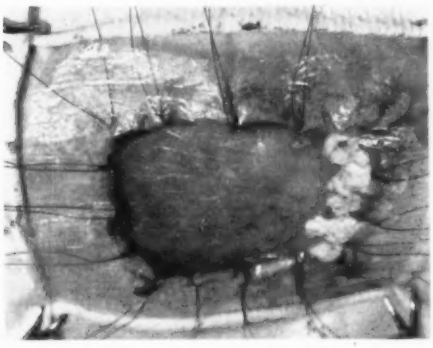


Fig. 2.—Gelatinous autograft particles ready to be spread over the skin defect.

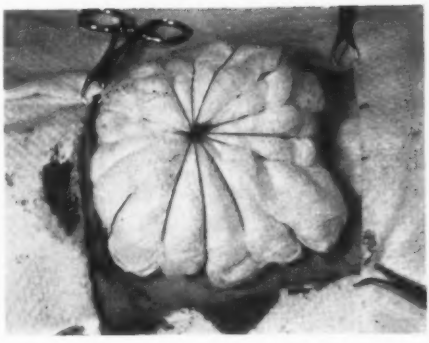


Fig. 3.—Gauze fluff pressure dressing in place.

producing a thin gelatinous suspension, ready for application to a full-thickness skin defect.

This defect was created by excising a full-thickness layer of skin and superficial fascia, measuring 10×10 cm. at the site where the split-thickness skin graft had previously been taken. This excision was carried down to the fascia overlying the skeletal muscles. The depth of the excision of the skin was verified by biopsy. This ensured excision of all epidermal components, precluding the possibility of regeneration of epithelium from these elements to invalidate the percentage of graft take. After creating the defect, hemostasis was obtained by using 0000 black silk ligatures. The skin edges were fixed to the fascia by means of interrupted black silk sutures.

The thin gelatinous autograft particles were spread over the skin defect in a smooth, thin layer, using a knife handle (Fig. 2). The defect was covered with a sheet of transparent plastic that had been perforated many times with a hypodermic needle to permit fluid to escape from the defect. This afforded a transparent window, through which the early progress of the graft could be observed without disturbing the graft itself. The plastic sheet was covered with sterile gauze fluffs, and these were secured in place with stent sutures from the wound edges (Fig. 3). The control animals were treated similarly except that no skin graft was applied to the defects that were created.

The success or failure of the homogenized autograft was determined by serial biopsy specimens taken on the 7th, 14th, 21st, and 28th postgraft days (Figs. 4, 5, and 6). The biopsy tissue was taken from the center of the grafted area to obviate inclusion of epithelial ingrowth from the wound edges. Biopsy was facilitated by excising the fascia overlying the skeletal muscle. The viability of the epithelium obtained at biopsy was

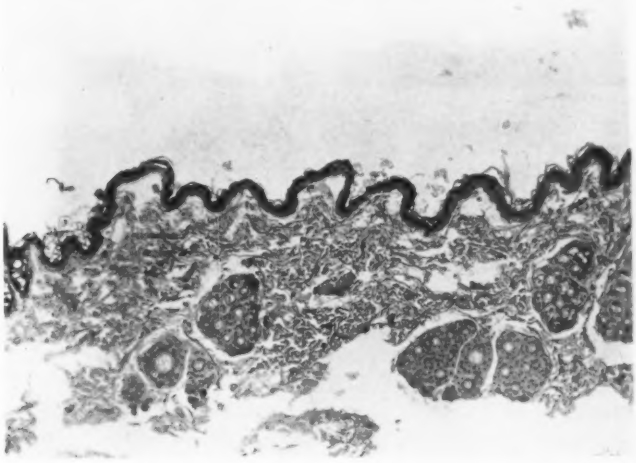


Fig. 4.—Biopsy tissue of normal rabbit skin.

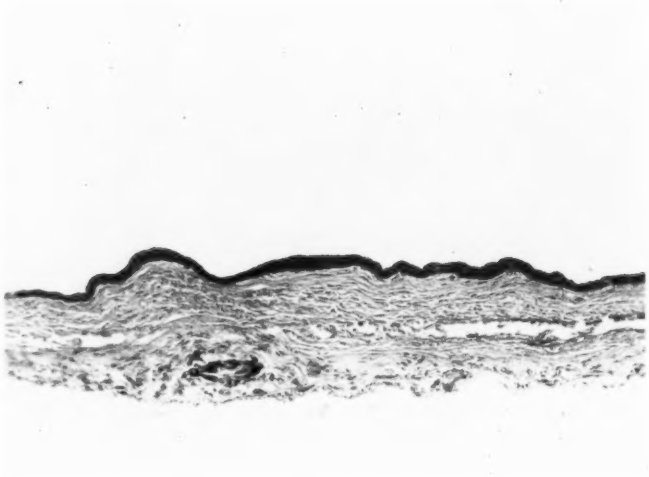


Fig. 5.—Biopsy tissue of center of defect one week after grafting.

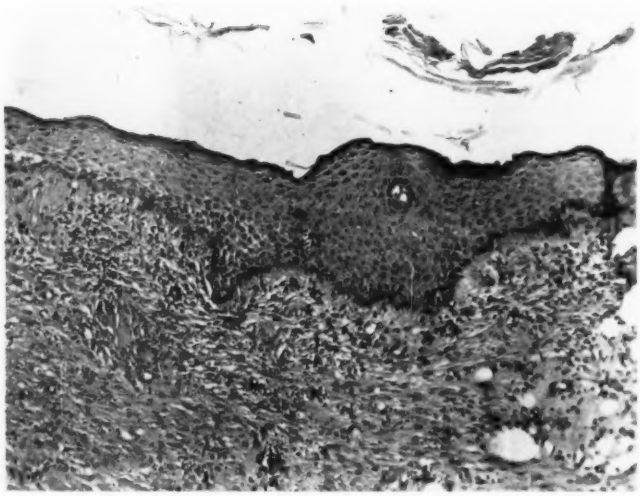


Fig. 6.—Biopsy tissue of center of defect three weeks after grafting.

determined by the following indices: (1) sharp outline of the nuclear membrane; (2) intact nuclear chromatin network; (3) absence of pyknosis, karyorrhexis, and karyolysis, and (4) actively advancing epithelial edges.

The percentage of the graft take was determined by clinical observation in conjunction with viable biopsy tissue. Autopsies were performed on all animals that died. Cultures were obtained from those grafts that became clinically infected.

Results of Fine-Particle Skin Autograph Technique in Rabbits

	No. of Animals	No. of Anesthetic Deaths	Viable Grafts	Infection of Graft Site	Healed at 3 Wk.	Average Size Defect at 3 Wk., Sq. Cm	Healed at 4 Wk.	Average Size Defect at 4 Wk., Sq. Cm
Grafted	30	4	21	7	9	52	20	11
Control	10	2	0	2	0	56	0	12

Results

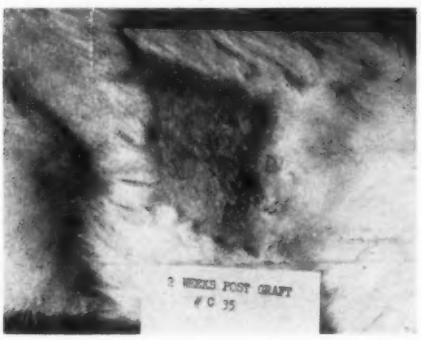
The accompanying Table records the results of these studies. Four of the grafted animals died of anesthesia and were excluded from the study. Viable grafts were obtained on 21 of the 26 animals grafted. Nine of the grafted animals had complete healing three weeks after grafting. Twenty of the grafted animals had complete healing four weeks after grafting. None of the control animals were healed at four weeks, and the average time of complete healing of these animals was seven weeks, with a range from six to eight weeks.

There was marked contraction of the original 10×10 cm. defect in both the grafted and the control animals. The defect in all animals consistently contracted to approximately 50% of its original size in two weeks and to 10% of its original size in four weeks (Figs. 7 and 8).

By observing the fluid present under the transparent plastic and present in the gauze fluffs at dressing changes, it appeared that the application of the homogenized skin did not stop the loss of fluid from the defect.

Twenty-seven per cent of the grafted animals developed infection at the graft site, as evidenced by lysis of skin particles, purulent exudate, edema, erythema, and odor. The micro-organisms most commonly cultured were Micrococcus pyogenes and Pseudomonas aeruginosa.

Fig. 7.—Grafted defect two weeks after grafting almost completely healed.



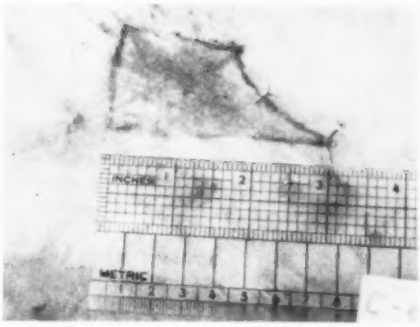


Fig. 8.—Grafted defect three weeks after grafting completely healed.

Four rabbits died in the postgraft period prior to complete healing. Three of these were from the control group, and one was from the grafted group. Autopsies on these animals revealed findings compatible with septicemia.

The scars of both the grafted and the control animals were firmly attached to the underlying fascia after complete healing. The grafted sites appeared to tolerate trauma well after complete epithelization. This coverage was evaluated by abrading the grafted area with a blunt instrument and observing the effects of cage life on the grafted area.

Comment

It was difficult to determine the amount of skin coverage obtained because of the continued contraction of the size of the defect. This marked contraction results from the loose attachment of rabbit skin to the underlying fascia. Unless this factor is taken into consideration when one is evaluating the area covered in grafting experiments on rabbits, erroneous conclusions will be drawn.

Three weeks after grafting, if the defect had contracted to 6×7 cm. and was 60% covered with skin, then the actual area of grafted skin was 6×7 cm. times 60%, or 25 sq. cm. This is approximately 2.5 times the area of the skin graft that was minced in the Blendor and applied to the defect.

The increased edge surface of the multiple small particles of homogenized autograft

permitted epithelization to proceed from multiple points. This may explain this increase in area coverage.

Many of the epithelial cells of the graft were broken up by the blades of the Blendor or sufficiently traumatized to cause death, and this may be the reason why an even greater coverage was not obtained. Stained smears made of the suspended skin particles after blending revealed fragmentation of many cells. Usually the fragments were composed of groups of cells and occasionally an intact hair follicle. Hair follicles were also seen in the biopsy specimens obtained from the center of the grafts. In rare instances fine hairs were found growing in the graft area.

Since this technique does not give complete epithelial coverage initially or for several weeks after grafting, there are raw areas remaining that result in loss of fluids and provide portals of entry for invasive micro-organisms.

This grafting technique would seem to be unsuited for primary coverage around joints or in regions where elasticity is necessary. However, it might be of value in providing coverage for large, immobile areas. Cosmetically it leaves much to be desired.

Summary

1. Split-thickness skin autografts will survive five minutes of mincing in a food Blendor, and the cell homogenate will proliferate when placed on a raw defect.

2. This fine-particle technique of skin grafting covers approximately 2.5 times as much area as the solid-sheet split-thickness skin-grafting technique.

3. In the rabbit, a marked contraction of full-thickness defects occurs as healing takes place because of the loose attachment of rabbit skin to the underlying fascia. Within two weeks the defect is only one-half its original size; in four weeks, only one-tenth. Unless this factor is considered in evaluating the area covered in skin-grafting experiments on rabbits, erroneous conclusions will be drawn.

4. The fine-particle skin graft technique does not appear to prevent fluid loss early in the course of the graft. Apparently it does not prevent infection.

5. In using this technique, marked contraction and fixation of the scar are seen. It could not be expected to give satisfactory results in areas where mobility is required, such as areas around joints. It might be of value in providing coverage for large, immobile areas.

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Evaluation of Surgical Approaches to the Mitral Valve

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Introduction

Techniques for direct-vision repair of the commoner congenital lesions of the right side of the heart are being standardized, and increasing attention is being directed to the left side of the heart. Utilizing cardiac arrest, the aortic valve may be explored fairly easily, and mitral stenosis and insufficiency are being corrected clinically. Unfortunately, acquired lesions of the aortic valve are difficult to repair adequately, and, in addition, aortic insufficiency presents a special problem in that the heart is difficult to arrest, in the first place, and then difficult to restart, in the second. This is due to poor coronary artery perfusion, resulting from the incompetent aortic valve. Mitral stenosis and insufficiency present a more encouraging picture because in most instances the changes in the valve are more amenable to surgical correction than those of the aortic valve and the problems related to cardiac arrest differ from those associated with aortic insufficiency.

Although certain techniques for open surgery of the mitral valve have already been utilized clinically,[4] it is the purpose of the present study to evaluate critically such techniques from the standpoint of (1) ease of application, (2) adequacy of valve exposure, (3) necessity for adjunct cardiac arrest, and (4) incidence of air embolus.

Methods

Both acute and survival experiments were carried out in healthy, anesthetized mongrel dogs in which thoracotomy incisions were made through either the right or the left fifth interspace, or transsternally through the fifth interspace, depending upon the experimental approach. During periods of cardiac bypass and intracardiac surgery, cardiopulmonary function was maintained by means of a rotating disc oxygenator coupled with a Sigmamotor pump. Perfusion rates ranged from 60 to 80 cc. per kilogram per minute.

Cardioplegia was obtained by injecting potassium citrate, 2 cc. of 2.5% of solution diluted to 20 cc. with oxygenated blood, into the base of the aorta after cross clamping the ascending aorta. The potassium solution was injected in amounts just sufficient to obtain cardiac arrest.

Periods of cardiac bypass ranged from 10 to 30 minutes. Various manipulations, such as placing sutures in the valve annulus, were carried out to simulate clinical maneuvers while the mitral valve was exposed. During such manipulation of the valves the left ventricle was of necessity emptied, the blood being replaced by air.

It became apparent soon after the inception of the study that consistent success or failure of a technique depended mostly on the incidence of air embolus, which, in turn, depended upon how well the left ventricle could be evacuated of residual air before the bypass was terminated. The ease with which the air could be completely removed from the left ventricle depended, in turn, upon whether the left ventricle was primarily dependent or superior in position during the open cardiotomy. To evaluate this principle, anatomical studies were carried out to establish the relationship of the various valves and chambers during open cardiotomy. Both survival and acute experiments were carried out. The incidence of air embolus was determined by noting air in the coronary vessels during surgery and in the cerebral circulation at postmortem examination.

Three approaches to the mitral valve were studied: (1) right-sided approach through a unilateral right thoracotomy incision entering the left atrium through the interatrial sulcus; (2) left-sided approach through a transsternal incision entering the left atrium from the left side by means of an incision in the left atrial appendage; (3) left-sided approach through a unilateral left thoracotomy incision with both partial and total cardiac bypass.

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From the Department of Surgical Research in the Division of Surgery, St. Luke's Hospital.

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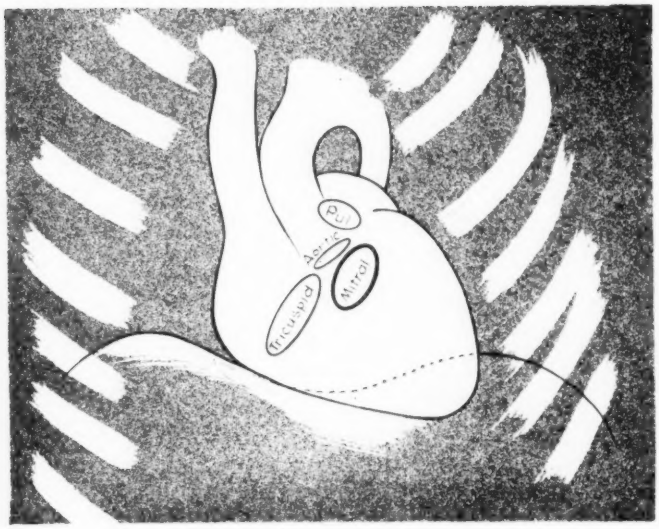

Fig. 1.—Relative positions of the valves of the heart superimposed on the profile of the heart viewed anteriorly.

Results

1. Unilateral Right Thoracotomy Incision; Left Atrium Opened from Right Side.—This undoubtedly represents the best surgical approach to lesions of the mitral valve. After the usual cannulations were made, and before placing the animal on the bypass circulation, the left atrium was exposed by dissection in the interatrial sulcus to allow a larger incision in the left atrium. Adjunct cardiac arrest was not used, nor would it be necessary unless a concomitant aortic insufficiency should exist.

With this approach the mitral valve lies at some distance from the site of the atriotomy incision (Fig. 1), so that exposure and visualization of the valve in the normal-sized left atrium may be somewhat limited. It is, however, satisfactory. The posteromedial commissure of the valve is nearest the incision, hence the most easily visualized. This is, of course, of some advantage in the treatment of mitral insufficiency, in which sutures are placed in the posteromedial commissure. With the right-sided approach, associated lesions of the aortic and tricuspid

Incidence of Air Embolus Encountered in the Various Approaches to the Mitral Valve in Dogs

Approach	Cardiac Arrest	No. of Dogs: Acute Exper.	Survival Exper.	Air Embolus	Survival *
Right thoracotomy: Left atrium opened from right side	No		6	0	6
	No	7		0	7
Transsternal: Left atrium opened from left side					
(*a*) Left ventricle vented	Yes	6		0	6
	No	2		0	2
(*b*) Left ventricle not vented	Yes	6		4	3
	No	2		1	2
Left thoracotomy					
(*a*) Total bypass	No	4 †			
(*b*) Partial bypass	No		7 ‡	3	3

* Survival in acute experiments means recovery of cardiac function to preoperative level prior to killing the animal.
† All experiments were technical failures.
‡ One experiment was a technical failure.

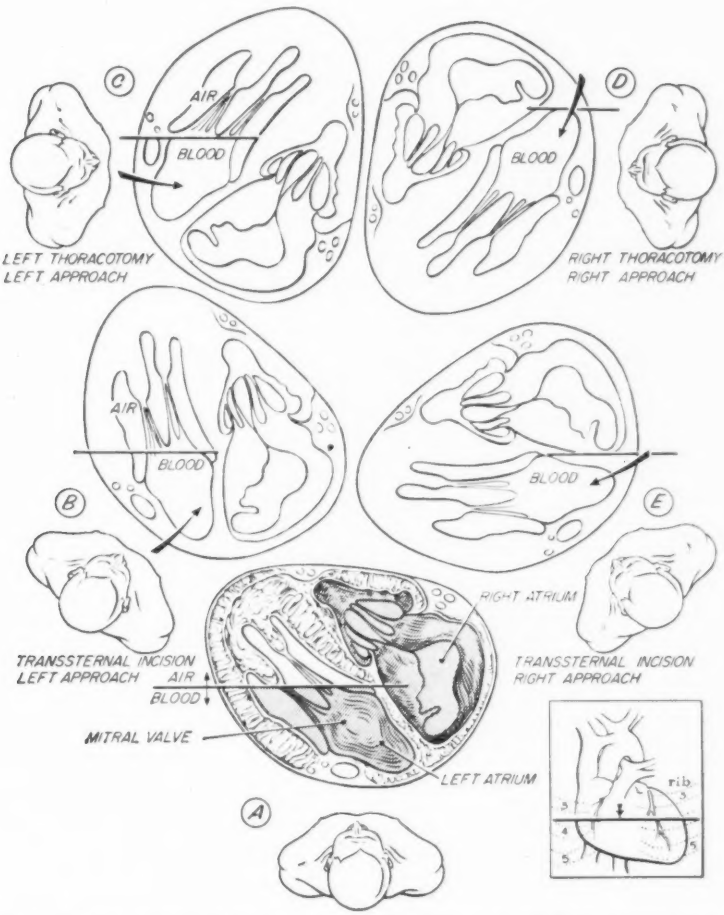

Fig. 2.—Sagittal sections of the heart at the level depicted in the insert, viewed from above with the patient positioned as shown. The arrows indicate the approximate approach to the mitral valve; the air-blood levels, the possibility for trapping residual air in the left ventricle.

valves are likewise readily accessible for surgical correction.

Air embolus is not a problem when the mitral valve is exposed in this manner. There was not a single instance of embolus found in a total of 13 dogs. Six of these animals survived 24 hours or more, and 7 were killed and examined immediately for air at the termination of the experiment (Table). An explanation of the absence of air emboli in these dogs is apparent when Figure 2*D* is studied. With the animal placed on its left side on the operating table, the left ventricle is the most dependent portion of the heart. Residual air is not trapped, therefore, in the ventricle or the aortic outflow tract when the heart refills during closure of the left atrial incision. This is likewise true, but perhaps to a less extent, when a transsternal incision is made and the mitral valve approached from the right side with the patient in a 45-degree supine position (Fig. 2*E*).

An added advantage of the right-sided approach to the mitral valve lies in the fact that any blood returning to the left side

of the heart tends to pool in the left ventricle without flooding the valve area, affording better visualization of the valve during surgery. It is a simple matter to allow the left side of the heart to fill prior to closing the left atrial incision, and, as it does, all of the air is forced out of the left side of the heart through the incision placed in the most superior position. When the left atrium is completely filled with blood, the atriotomy incision is closed, while blood leaks from the incision to avoid trapping even a minimal amount of air.

II. Transsternal Incision; Left Atrium Opened from Left Side.—The ease of applicability of this approach is similar to that through a unilateral right thoracotomy incision except that the transsternal incision is more extensive and necessitates opening both pleural cavities. In some experiments a vent was placed in the left ventricle by way of the left atrial appendage to remove residual air during closure; in others the left atrium was closed without venting. The venting technique is simple. Just prior to closing the left atrium, a No. 14 F. plastic cannula* is inserted through the mitral valve into the left ventricle. The atrium is closed about the catheter, which is connected to gentle suction. After all the air is removed from the left ventricle, and just prior to taking the heart off pump support, the catheter is removed, with the suction maintained.

Because the apex of the heart tends to rise with the pericardium open, visualization of the mitral valve may be no easier from this approach than from the right side. When exposure is obtained, however, it is somewhat easier to work on the valve, since it is closer to the atriotomy incision (Fig. 1).

With a competent aortic valve, cardiac arrest is not mandatory, but exposure of the mitral valve is greatly simplified in the flaccid, nonbeating heart. In addition, residual air in the left ventricle may be massaged from the flaccid heart during closure. At any rate, cardiac arrest is a more necessary adjunct for proper exposure of the valve from the left side than from the right. With this approach, the left atrium is the dependent chamber, so that blood returning through the pulmonary veins pools here and tends to obscure the operative field more than when the valve is approached from the right. Because the left atrium is in the dependent position, much of the left ventricle is superior to it, and air may be trapped in this chamber and in the aortic outflow tract

*C. R. Bard, Inc., Summit, N. J.

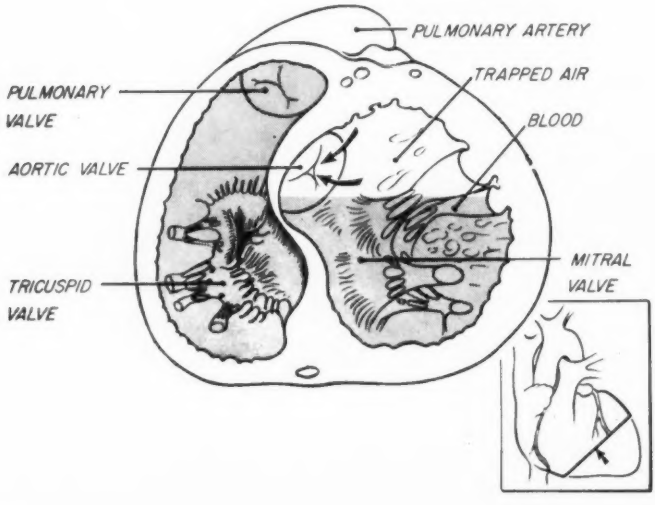

Fig. 3.—Sagittal section of the heart at the level shown in the insert, viewed from below to show the relationship of the mitral valve and the aortic valve to the residual air bubble in the left ventricle.

during closure of the left atrial incision (Figs. 2*B* and 3). For this reason, unless the left ventricle is adequately vented, the incidence of air embolus is prohibitively high, as shown in the Table. Five out of a total of eight dogs in which the left ventricle was not vented showed evidence of air embolus after left cardiotomy. On the other hand, the incidence of air embolus in the eight dogs in which the left ventricle was properly vented was zero. Embolization of air almost always occurred during the first few vigorous cardiac beats, when the heart takes over the circulation after the pump is turned off. Occasionally, it will occur prior to this if pump speed is reduced slowly and the left ventricle is able to eject blood and air against the pressure head created by the pump.

III. Unilateral Left Thoracotomy Incision; Left Atrium Opened from Left Side.

Because it is desired to open only one side of the chest during mitral valve surgery, techniques to approach this valve through a left thoracotomy incision were also studied. Two methods were evaluated, one involving total cardiopulmonary bypass, the other bypassing only the lungs and the left side of the heart. As can be seen by studying Figure 2*C*, the left ventricular chamber is again superior in position with this approach, and problems of air embolization are similar to those discussed in the preceding section.

A. Complete Cardiopulmonary Bypass: Although it is possible to accomplish a total cardiopulmonary bypass through a left thoracotomy incision, the technique is difficult and should not be considered too seriously at the present stage of experience. The vena caval catheters are passed through the tip of the right atrial appendage, which is just barely visible and which can be drawn into the operative field. Proper placement of the catheters in the superior and inferior venae cavae is difficult. It is not necessary to place occluding tapes around the caval catheters, since by keeping the vena caval pressures low and the cavae partially collapsed, the right side of the heart is maintained empty, blood being prevented from passage through the lungs. If cardiac arrest is utilized, the latter consideration is not important.

B. Bypass of Lungs and Left Heart Only: This technique necessitates the construction of a special plastic cannula, similar to that previously described [1,2] to be inserted into the right ventricle by way of the pulmonary outflow tract. The cannula is held in place by means of purse-string sutures. Overdistention of the right ventricle can be avoided either visually or by means of a pressure cannula incorporated in the inflow cannula in the right ventricle. Seven dogs were operated on utilizing this technique. Cardiac arrest was not used. In each instance the mitral valve was exposed, the exposure being adequate. Surgery was carried out successfully in three of the seven dogs, and the dogs survived for periods of over 24 hours. In three dogs, the perfusion was satisfactory, but irreversible ventricular fibrillation occurred, owing to air emboli in the coronary arteries forming immediately after the pump was stopped and the heart took over its own function. One experiment was a technical failure. All in all, the technique was considered to be a poor way by which to approach the mitral valve, since it requires special techniques and is more difficult to utilize than total cardiopulmonary bypass.

Comment

Open techniques for mitral valve surgery will gradually replace existing closed techniques as the open methods continue to become safer in their application. In spite of efficient pump oxygenators and well-trained surgical teams, the specter of air emboli in vital organs remains as an unexpected catastrophic event. The ease of application of a technique and the adequacy of valve exposure become secondary considerations if the technique cannot be applied without the fear of air emboli.

Because the large diseased hearts found in adults with acquired heart disease are

more susceptible to the complications of cardiac arrest, it is important to be able to expose the mitral valve adequately without the adjunct of cardioplegia, except in imperative situations.

In these experiments, the right-sided approach for surgery of the mitral valve proved to be the most satisfactory from all standpoints. Only a unilateral right thoracotomy incision is necessary; visualization of the valve is adequate; cardiac arrest is not mandatory, and of utmost importance is the fact that the incidence of air embolus was zero. There is the added advantage that associated lesions of the aortic and tricuspid valves likewise are accessible for surgical correction.

Unless the left ventricle is properly vented, left-sided approaches to the mitral valve are associated with a prohibitively high incidence of air embolus. In addition, cardiac arrest is more imperative as an adjunct procedure to gain proper visualization of the mitral valve. With the left ventricle vented to avoid trapping of air in this chamber, overdistention of the left ventricle during recovery from cardiac arrest is likewise prevented. In these experiments in which the left ventricle was vented, recovery from potassium-citrate-induced cardiac arrest was 100%, which varies from results in previous work in which this factor of overdistention was not controlled.[3]

At the present stage of our experience, operations through unilateral left thoracotomy incisions can be discarded as inferior to those described above.

The experimental observations documented in this report have been confirmed in a small clinical experience involving both stenotic and insufficient mitral valves. At the present time all patients with mitral insufficiency are operated on utilizing open techniques in the repair of the valve. With mitral stenosis, the pump-oxygenator equipment and team are standing by, and, in the event that the valve cannot be opened satisfactorily by finger fracture, the patient is placed on cardiopulmonary bypass for commissurotomy under direct vision.

Summary

1. Techniques for satisfactory surgery of the mitral valve are evaluated.

2. The relationship of the position of the various chambers of the heart during surgery to the incidence of air embolus is stressed.

3. It is concluded that the right-sided approach to the mitral valve is most satisfactory from the standpoint of ease of application, adequacy of mitral-valve exposure, the fact that adjunct cardiac arrest is not necessary, and the absence of air embolus.

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Strangulated Internal Hernia Associated with Trauma

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Two patients with strangulated intestinal obstruction due to internal hernia associated with trauma admitted to the Third Surgical Service at St. Luke's Hospital aroused our interest in this condition, especially since the first of these patients is our father. Intestinal obstruction caused by internal hernia is relatively uncommon, the incidence ranging from less than 0.01% to 5% of all cases of acute intestinal obstruction in various series. Even more unusual are those cases with hernia through defects in the mesentery or omentum, such as occurred in the cases here reported. Excluding those defects produced surgically, these amount to about 10% of the reported cases of internal hernia.

Careful review of the literature revealed only 32 previous cases of hernia through a defect in the greater omentum (Table 1). The fine review by Martzloff [16] covered the period from 1840 to 1929, and three other authors reviewed the literature, but only one article contributed more than a single original case. In addition to the single case added herein, six cases not included in any previous review articles were collected.

In none of the reported cases was the omental defect considered to be of traumatic origin, although this was mentioned as a possibility in one of Martzloff's collected cases, with no details given. Lifting injuries were associated with the onset of symptoms in the first two cases listed, but these were not considered sufficient to produce the defects. Our first case is therefore unique in being the first reported instance of transo-

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TABLE 1.—*Transomental Hernias*

Author	Original Cases	Cases from Literature, Not Included in Prior Reports
Copenhaver	1	
Kirchner †	1	
Martzloff *	1	17
McIver †	1	
McLean	1	
Gentile	1	
Hansmann and Morton *		1
Mayo, Stalker, and Miller †	1	
Sanes and Postoloff *	1	5
Gubler and Yedinak *	1	
Davies †	2	
Mock and Mock †	1	
Total	12	21
Grand total	33	

* Collective review.

† Cases not included in any reviews, totaling 6.

TABLE 2.—*Transmesenteric Hernias*

Author	Original Cases	Cases from Literature, Not Included in Prior Reports
Fritz *		46
Mayo	2	
Rutherford	1	3
Kirchner †	1	
Short *		11
Brown *	3	11
Richardson †	1	
Cutler *	2	5
Short		3
McIver †	2	
Smith, A. M. *	1	8
Edwards *	2	1
Hunter †		3
Gatewood *	2	3
Jackson †	1	
Workmen's Compensation Acts †	1	
Hansmann and Morton *	1	4
Cutler and Scott *	2	3
Dolton †	1	
Smith, R. †	1	
Tanner †	2	
Johnson †	1	
Mock and Mock †	1	
Total	26	101
Grand total	127	

* Collective review.

† Cases not previously included in any reviews, totaling 15.

mental hernia in which the defect and hernia were produced by injury.

One hundred twenty-six cases of intestinal obstruction due to herniation through nonsurgical defects in the mesentery of the small or large bowel were collected on thorough review of the literature (Table 2). This survey went back as far as 1836 in the excellent collective review by Prutz.[21] To these we add one case. No author has added more than two new cases, most instances being covered in single-case reports. Occasional comprehensive reviews have appeared, as noted in the Table, the latest being that of Cutler and Scott [8] in 1944. It is difficult to collect all of the scattered cases, and no author has been completely successful. Hansmann and Morton [11] tabulated 132 transmesenteric hernias, but their sources were not clear, so that duplications may have been included. Gatewood [8] studied this situation carefully and reported 69 cases up to 1934, including 13 cases which had never previously been collected. Nonetheless, 18 cases were found reported prior to that time which he failed to include, 10 by Prutz and 8 elsewhere (the 7 original cases reported by Mayo, Kirchner, Richardson, McIver, and A. M. Smith, and one of the two cases of Hommes collected by Smith). We have also added seven isolated cases reported since 1934 and not previously collected.

In only 12 of these cases of transmesenteric hernia was a history of trauma obtained (Table 3), including even remote, minor injuries possibly related to the cause of the hernia but not to the production of the defect. Straining that seemed quite definitely the precipitating cause of the hernia occurred in the Workmen's Compensation Acts report,[30] as well as in our case. Only in the single cases of Kirchner [15] and Brown [1] did the mesenteric defect appear to be of traumatic origin.

TABLE 3.—*Transmesenteric Hernias Related to Trauma*

Author	Minor Injuries Possibly Related to Production of Hernia But Not of Defect	Injuries Which Produced Defect
Prutz	4	
Rutherford	2	
Kirchner		1
Brown	3	1
Cutler	2	
Workmen's Compensation Acts	1	
Mock and Mock	1	
Total	13	2

It is thus apparent that omental or mesenteric defects through which such hernias occur are rarely caused by trauma. It is the consensus that such defects are usually developmental in origin, although they are occasionally the result of inflammation.

These defects are much commoner than hernias through them resulting in obstruction. Free passage of the intestine through the defect and back again by peristaltic action probably occurs, with no symptoms unless incarceration develops. Strangulation usually occurs early. The lack of any pressure differential between the two sides of the defect within the abdomen, even with the application of external forces, accounts for the relative infrequency of this condition and the rarity with which it follows trauma.

The preoperative diagnosis, beyond that of intestinal obstruction, is extremely difficult to establish in internal hernias and was not made precisely in any of these collected cases. The early onset of strangulation is indicated by the 75% to 80% incidence of this condition. Of the 22 cases of transomental hernias in which the condition of the bowel was stated, 55% had strangulation without necrosis, and an additional 27% had gangrene. Forty-three such cases of transmesenteric hernia had 26% strangulation and 49% gangrene. Results of treatment of 26 collected cases of transomental and 95 cases of transmesenteric hernia in which sufficient data were presented are summarized in Tables 4 and 5. The improvement in the mortality rates

TABLE 4.—*Transomental Hernias*

	Prior to 1936			Since 1936			Total		
	Cases	Died	Mortality Rate	Cases	Died	Mortality Rate	Cases	Died	Mortality Rate
Surgery performed	17	3	18%	5	0	0	22	3	14%
Bowel resection—all gangrenous	3	2	67%	2	0	0	5	2	40%
Reduction of hernia	10	0	0	3	0	0	13	0	0
Strangulated but viable	6	0	0	3	0	0	9	0	0
Circulation unimpaired	4	0	0	—	—	—	4	0	0
Type of surgery and condition of bowel not stated	4	1 *	25%	—	—	—	4	1	25%
No surgery	3	3	100%	1	1 †	100%	4	4	100%
Bowel gangrenous	1	1	100%	—	—	—	1	1	100%
Strangulated but viable	2	2	100%	1	1	100%	3	3	100%
Total	20	6	30%	6	1	17%	26 ‡	7	27%

* Pathology not detected at surgery; patient died with gangrenous obstruction.
† Moribund on admission due to strangulated obstruction.
‡ Of 33 total cases, 26 cases in which end-result was stated.

since 1936 indicates the great advances in surgical therapy in recent years, particularly in those cases requiring resection. The major reason why 33 cases had no surgery, with a 100% mortality rate, was deterioration of the patient's condition beyond the point where indicated surgical procedures could be tolerated. Early diagnosis, necessary supportive care, and prompt surgical intervention before this state is reached are the major factors in lowering the excessive mortality rate.

TABLE 5.—*Transmesenteric Hernias*

	Prior to 1936			Since 1936			Total		
	Cases	Died	Mortality Rate	Cases	Died	Mortality Rate	Cases	Died	Mortality Rate
Surgery performed	45	23	51%	9	1	11%	54	24	44%
Bowel resection—all gangrenous	12	6	50%	3	0	0	15	6	40%
Reduction of hernia	19	6	31%	6	1	17%	25	7	28%
Strangulated but viable	6	1	17%	2	0	0	8	1	13%
Circulation unimpaired	7	3	43%	4	1 *	25%	11	4	36%
Condition of bowel not stated	6	2	33%	—	—	—	6	2	33%
Laparotomy—procedure not stated	14	11	79%	—	—	—	14	11	79%
Bowel gangrenous—patient moribund—unfit for resection	3	3	100%	—	—	—	3	3	100%
Condition of bowel not stated	11	8	73%	—	—	—	11	8	73%
No surgery	29	29	100%	—	—	—	29	29	100%
Bowel gangrenous	2	2	100%	—	—	—	2	2	100%
Strangulated but viable	3	3	100%	—	—	—	3	3	100%
Patient moribund—condition of bowel not stated	1	1	100%	—	—	—	1	1	100%
No further details	23	23	100%	—	—	—	23	23	100%
Treatment not stated	12	6	50%	—	—	—	12	6	50%
Bowel gangrenous	1	1	100%	—	—	—	1	1	100%
Condition of bowel not stated	11	5	45%	—	—	—	11	5	45%
Total	86	58	67%	9	1	11%	95 †	59	62%

* Died of unassociated perforated peptic ulcer.
† Of 127 total cases, 95 cases in which end-result stated.

Report of Cases

CASE 1.—H. E. M., a 68-year-old white male surgeon, almost immediately after returning unscathed from a three-month hunting trip in South Africa, sustained fractures of his sternum and four ribs in an automobile accident. He was hospitalized elsewhere for one week and made satisfactory progress. Seven days after the accident he had an attack of upper abdominal pain, accompanied by light-colored stools, from which he recovered shortly without treatment. Three weeks after injury, on Oct. 27, 1949, he awoke with severe colicky right upper quadrant pain which did not radiate. Tenderness was marked in the right upper quadrant with guarding, but there were no other abnormal abdominal findings; bowel sounds were normal. Pain was relieved for a few hours by atropine, only to return with increased severity. He was admitted to St. Luke's Hospital at 6:00 p. m. Abdominal examination revealed exquisite tenderness in both upper quadrants, with dullness and some rigidity in the right upper quadrant, but no palpable mass. There was no distention, and the bowel sounds were hyperactive but of normal pitch. Blood pressure was 150/70 and pulse 42. X-ray of the abdomen was essentially negative. The white blood cell count never exceeded 11,400. Four hours after admission constant severe pain with occasional cramps persisted in the right upper quadrant, accompanied by nausea and vomiting. Tenderness and rigidity increased, and rebound tenderness developed. The pulse ranged from 36 to 48 until meperidine (Demerol) intravenously relieved pain, when his pulse rose to 130. The blood pressure fell to 60/0 at 3:00 a. m., and no blood pressure or pulse was obtainable at 6:00 a. m., in spite of intravenous fluids. Plasma and blood intravenously gradually raised his blood pressure, but tachycardia persisted and dehydration increased. Bowel sounds became faint and infrequent.

At 2:00 p. m., as soon as his condition permitted, abdominal exploration was carried out under general anesthesia. The diagnoses entertained preoperatively were acute cholecystitis with possible perforation, perforation of duodenum, hepatic or retroperitoneal hematoma, and mesenteric thrombosis. The correct diagnosis was not considered, although the patient later stated that he strongly suspected it.

At surgery, through a right subcostal incision, a considerable quantity of bloody peritoneal fluid was encountered, and a large mass of black, necrotic, dilated, fluid-filled bowel presented. The gangrenous small intestine was found to have herniated through a tear in the omentum which was fixed to the anterolateral aspect of the right lower quadrant by scarring from an appendectomy performed 36 years earlier. About 4 ft. of necrotic small intestine was rapidly resected and continuity restored with a side-to-side anastomosis.

General improvement was immediate, but convalescence was slow because of complications: atelectasis on the third day after surgery; weakness and mental confusion, attributed to toxemia, cerebral anoxia, and medication, and left upper quadrant pain on the 11th postoperative day, due to anastomotic leak or partial obstruction. Penicillin and chlortetracycline (Aureomycin) were administered in spite of his known sensitivity to penicillin; Tripelennamine (Pyribenzamine) was given prophylactically. There was some evidence of cardiac decompensation, which was controlled medically, but there was considerable difficulty in maintaining his fluid and electrolyte balance without overloading his circulatory system. His electrocardiogram revealed no changes.

He was discharged from the hospital on his 33d postoperative day, but was readmitted 16 days later because of agranulocytic angina. No polymorphonuclear neutrophils or band forms were present. This was attributed to tripelennamine, the only medication he continued after his initial hospital stay. The white blood cell and differential counts had returned to normal when he left the hospital, 12 days later. He has had no further gastrointestinal symptoms, although an incisional hernia developed and persists.

CASE 2.—N. G., a 62-year-old white male merchandise buyer, suddenly developed cramping abdominal pain, followed by nausea and vomiting, while strenuously chopping wood on Aug. 22, 1952. He was hospitalized elsewhere the next evening because of constant abdominal pain, with intermittent cramps, and vomiting, not relieved by a normal bowel movement and passing small amounts of flatus. He had had no previous gastrointestinal symptoms or abdominal surgery, and there was no weight loss. There was a history of nephritis in 1932, with persistent hypertension. Barium enema revealed a large lesion of the sigmoid colon, and he was transferred to the Third Surgical Service at St. Luke's Hospital by ambulance on Aug. 26.

Examination on admission revealed a tensely distended, tympanitic abdomen, with diffuse tenderness but no palpable masses. Bowel sounds were active and tinkling. Rectal examination was negative. Dehydration was obvious. His blood pressure was 170/88 and his pulse 68. A harsh systolic murmur was heard. The white blood cell count was 4150.

X-rays of the abdomen revealed a small-bowel obstruction. A Cantor tube was passed successfully. Surgery was accomplished on Aug. 29. From 12 to 15 ft. of small bowel was herniated and incarcerated through a 3¼ in. rent in its

mesentery. The herniated intestinal loops were dilated and dark, but the bowel appeared viable after reduction of the hernia. A transverse colostomy was performed in the right upper quadrant because of the lesion noted on the barium enema.

His postoperative course was somewhat difficult, with an episode attributed to a pulmonary embolus. Electrolyte balance was maintained with difficulty because of a low-sodium diet for two months prior to surgery. The electrocardiogram on two occasions was within normal limits. The Cantor tube was removed and the colostomy opened on the sixth postoperative day.

He was discharged from the hospital on Sept. 22 and readmitted on Nov. 30. Barium enema at this time revealed no lesion of the sigmoid. The colostomy was closed on Dec. 12, and he went home six days later. He returned to work on Jan. 5, 1953, and he remains active, with no gastrointestinal symptoms and with normal bowel habits.

Comment

These two cases of strangulation obstruction due to internal hernia, one transomental and one transmesenteric, are quite typical of those reviewed. The associated trauma makes them unusual. The appearance of the omental defect indicated that it was traumatic in origin, the first such lesion reported. It was comparable to the only two traumatic mesenteric defects described, those reported by Kirchner and Brown. The mesenteric defect presented herein was thought to be congenital, but the minor trauma was considered sufficient to have precipitated the obstruction.

As has been true of all such cases, accurate diagnosis was not made preoperatively in either of these instances. The first was not even recognized as intestinal obstruction, and the patient's condition deteriorated so rapidly that it could barely be restored sufficiently for surgery. Resection was successful, but survival was considered most fortuitous. Expert anesthesia, antibiotics, and accurately controlled intravenous fluid and electrolyte therapy are invaluable. Intestinal intubation and suction may avoid further distention and edema and delay gangrene while indicated supportive care is rapidly administered preoperatively, and they are valuable adjuncts postoperatively. Strangulation occurs so early in these cases that suction has no place in their definitive treatment. The importance of early diagnosis and prompt definitive surgery is emphasized. Only thus can reasonable mortality rates be obtained.

Summary

Intestinal obstruction due to internal hernia through a defect in the mesentery or omentum was found to be relatively rare on careful review of the literature. Thus 33 cases of transomental hernia and 127 cases of transmesenteric hernia were collected.

Such mesenteric and omental defects are usually developmental, and occasionally inflammatory in origin. Trauma is rarely associated with such hernias, particularly in the production of the defect.

A case of strangulated transomental hernia, in which both the omental defect and the hernia were attributed to injury, is presented. Surgical treatment, consisting of resection of about 4 ft. of gangrenous small intestine, was successful in spite of several complications.

Also reported is a case of strangulated transmesenteric hernia. Trauma apparently precipitated the hernia through a developmental defect. Reduction of the viable bowel was accomplished surgically, with recovery.

The etiological mechanisms of these hernias is not entirely clear but primarily involves incarceration. This explains the high incidence of strangulation and gangrene. Precise diagnosis has never been made preoperatively in such cases. A high index of suspicion and early surgical intervention are essential for successful treatment, as indicated by the cases presented and analysis of the collected cases.

C. E. Shannon, M.D., and A. R. Morrow, M.D., gave us permission to report these cases.

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Cervicomediastinal Cystic Hygroma Associated with Chylopericardium

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Cervicomediastinal cystic hygroma is a rarely encountered pathological entity. Gross and Hurwitt [1] found 19 cases in the literature and added 3 of their own. The lesion in the case to be reported appears to be the second mediastinal hygroma associated with chylopericardium and the third case of spontaneous chylopericardium recorded.

The hygromatous cyst, typically, is a lobulated, thin-walled translucent sac lined by flattened endothelium. The lobules are usually separated by fibrous septa, but there may be free communication between them. The contained fluid is thin, clear, and faintly yellow. The lobules may extend between muscle bundles, nerve fibers, and other anatomical structures in the involved area. Goetsch [2] postulated that outgrowths or cords of endothelial cells insinuate themselves between the anatomical structures and by collection of fluid force apart the walls of the cords, developing lumina, thereby distorting the surrounding anatomy.

Hygromas tend to develop in the neck and, less commonly, in the groin or retroperitoneal spaces. Thus, a definite relationship is established with two known embryonic structures; the lymphatic sacs of the neck and those of the iliac regions. Huntington [3] believes that the endothelial-lined sacs of lymph arise from mesenchymal tissue, coalesce, ramify, acquire lumina, and subsequently acquire communication with various veins. Sabin [4] differs and suggests that a small endothelial bud develops from the jugular vein, becomes detached, and develops as a primary lymphatic sac or bud. This structure is paired in the neck, leading to bilateral involvement. At about the same stage of development, similar buds arise in relation to the pelvic veins, thus allowing hygromas to develop in these areas. An explanation for the peculiar locations of these lesions is thus apparent, since true hygromas do not develop elsewhere, while lymphangiomata may develop anywhere.

Mediastinal cystic hygromas may be either completely intrathoracic or, more commonly, combined as a cervicomediastinal lesion. In the latter type the mediastinal component appears to be an extension of the cervical lesion along the sheaths of the great vessels into the chest. The purely mediastinal lesions seem to arise in some manner from sequestered celomic or pericardial tissue.[5] Some of the lesions have a stalk-like communication to the pericardium.

The rationale for early eradication of the lesion is cosmetic deformity, and obstruction and risks of suppuration within the lesion. Treatment modalities have run the gamut. Watchful expectancy, in the hope that the lesion will subside, is usually futile. If suppuration occurs, the patients that survive occasionally are fortunate enough to have the lesion disappear, owing to contraction following inflammation.[1]

Multiple aspirations may lead to suppuration and its accompanying risks.

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The opinions or assertions contained herein are private ones of the writers, and are not to be construed to be official or reflecting the views of the Navy Department or the Naval Service at large.

Fig. 1.—Age 12 hours. Cervical and axillary cystic hygromatous masses present at birth.

Sclerosing agents injected into the lesions have occasionally been successful but also may lead to complications. Suppuration is a risk, and the danger of injecting a necrotizing agent in proximity to the brachial plexus or the carotid vessels or jugular veins, producing thrombosis, is obvious. Moreover, if there is a direct communication to a vein, such a quantity of agent may be disastrous to the infant.

Radium therapy has not generally proved successful, owing to the suppuration which frequently occurs.[6] While Goetsch[2] and Singleton[7] have had satisfactory experience with roentgen therapy to the mediastinum and Portmann[8] with the use of radon seeds, the long-range hazard of radiation to growing infants markedly limits the dosage and location of the treatment ports.

Surgical excision in stages has been a successful form of treatment. The cervical portion of the lesion is removed first, and occasionally, in favorable lesions, it may be possible to continue the dissection through the thoracic inlet, removing all or most of the mediastinal component.[9] A separate thoracotomy is necessary for large remnants which persist. For purely intrathoracic lesions a thoracotomy is indicated, both for diagnostic and for therapeutic purposes.

In the absence of infection, the dissection is not difficult. In proximity to great vessels and nerves, there may be some difficulty in removing all the tumor, which has grown into inaccessible areas. In such cases, removing the bulk of the tumor suffices, and spontaneous obliteration of the remaining tumor seems to occur.[1] The larger the mass the easier the dissection, the multilobulated mass being a little more troublesome. If possible, it is best to avoid collapsing the lesion, as its mass aids in removal of prolongations and insinuating projections. In the region of the parotid gland, care in preserving the facial nerve is necessary. Similarly, the spinal accessory, phrenic, and vagus nerves should be preserved.

Report of Cases

A female infant with a birth weight of 7 lb. (3175 gm.) was delivered by low forceps after approximately 15½ hours of labor. The condition of the infant at birth was poor. There were huge, bulging bilateral cervical, axillary, and left subscapular subcutaneous cystic masses (Figs. 1 and 2). Respiratory distress developed during the succeeding eight hours, owing to tracheal compression by the large cervical tumor. Roentgen examination of the chest revealed poorly defined upper mediastinal widening. Surgical decompression of the neck was considered an immediate necessity.

First Operation.—Under nitrous oxide, oxygen, and ether endotracheal anesthesia, the cervical masses were easily excised through bilateral cervical incisions. The lesions were transected where they disappeared under the clavicle into the chest. It seemed prudent to defer excision of the mediastinal, axillary, and scapular masses. The masses were typical multicystic hygromas. The neck wounds were closed with drainage tubes beneath the flaps.

Postoperatively, the infant responded satisfactorily, having only moderate difficulty with

Fig. 2.—Age 2 months. Left subscapular cystic hygroma present since birth.

mucus. She nursed well and promptly gained weight. She was discharged on the 10th day. The wounds healed normally.

Second Operation.—Two months later the remaining masses in the axillae and scapular areas were excised through bilateral axillary incisions (Fig. 3).

The mediastinal widening remained unchanged postoperatively and during the succeeding months appeared to be insignificant. However, at 13 months of age the patient was admitted with severe respiratory distress, relieved partially by tracheostomy. X-ray examination demonstrated a large superior mediastinal mass, and iodized oil U. S. P. (Lipiodol) instillation revealed stenosis of the left main bronchus and tracheal compression (Figs. 4 and 5). Serial films revealed an unexplained variation in the

Fig. 3.—Age 2 months. Healed axillary and cervical wounds following staged excision of cystic hygroma.

size of the mediastinal mass. Atelectasis due to bronchial obstruction was considered a likely possibility. Thoracotomy was elected.

Third Operation.—A transverse sternum-splitting thoracotomy and mediastinotomy was performed. There was a large cystic hygromatous mass in the anterior superior mediastinum, extending over the upper pericardium and blending intimately with the thymus and overlying the lung roots bilaterally. It was intimately adherent to the innominate veins and superior vena cava and along the esophagus. This amorphous-shaped mass, consisted of somewhat spongy, soft tumor tissue, which on cut section

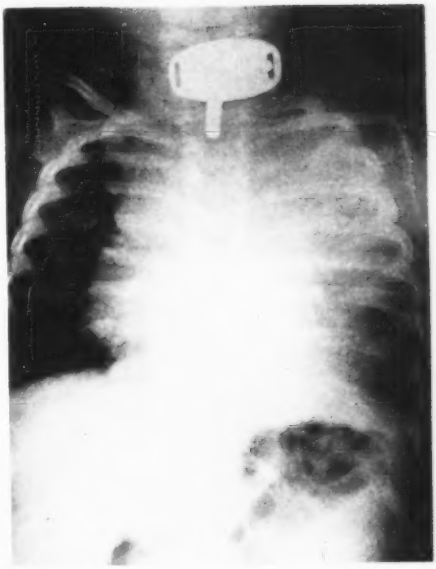
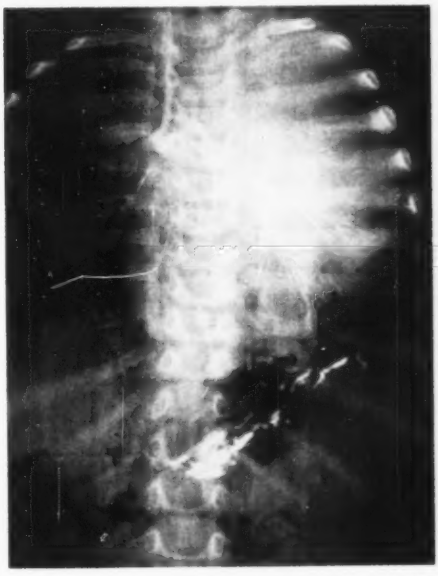


Fig. 4.—Age 13 months. Large mediastinal mass.

oozed fluid that in some areas appeared like lymph. The pericardium was moderately distended with approximately 150 cc. of thin white chylous fluid. This distention, plus the pressure of the overlying tumor mass, compressed the left main-stem bron-

Fig. 5.—Age 13 months. Bronchogram showing left main-stem bronchial narrowing.



chus and explained the abnormal-appearing bronchogram preoperatively. No gross intrinsic abnormality of the left main bronchus was noted. At the thoracic inlet, the hygromatous mass blended with the thymus and the lower poles of the thyroid gland and had a more fibrous and less cystic consistency.

The mass was dissected from the pericardium, phrenic nerves, esophagus, trachea, thymus, and thyroid gland, removing approximately 95% of the gross mass. The pericardial sac was aspirated through a 4 cm. incision, and no internal connection with the cystic tumor was noted. The pericardial incision was left open for drainage. The chest was closed in the usual manner with bilateral underwater drainage tubes.

The postoperative course was stormy, with repeated episodes of cyanosis and accumulation of chyle in the left chest. Repeated aspirations of the chest showed continuous filling with chyle, the nature of which was proved by demonstrating 144 mg. % of cholesterol, with a positive Sudan III stain for fat.

In spite of supportive measures, consisting of transfusions, antibiotics, tracheostomy toilet, and attempts to maintain nutrition, the patient died approximately three months from her last admission, being then 16 months old. Permission for autopsy was refused.

Comment

Groves and Effler [11] reported the first case of mediastinal hygroma associated with chylopericardium. They could find only six case reports in which chyle appeared in the pericardium, and in all these cases there was an associated massive chylothorax. Their patient was a 31-year-old woman with a hygromatous mass in the superior mediastinum, the fluid from which resembled lymph. The pericardial fluid was milky-colored chyle. They demonstrated Sudan III in the pericardial fluid eight hours after ingestion, thus proving the connection of the pericardium with the thoracic duct, despite the inability to demonstrate it at surgery. The hygroma was removed and the chylopericardium successfully controlled by ligation of the thoracic duct in the right chest at the level of the 10th thoracic vertebra. Touroff and Seley [12] controlled a chronic left chylothorax by ligating numerous lymphatic ducts in the mediastinum in a patient with lymphangiomatous transformation of the thoracic duct. Naef [13] reported a case of primary chylopericardium in a one-year-old girl successfully treated by transthoracic ligation of the thoracic duct.

Either mechanical obstruction of the superior vena cava by the tumor or lymphatic obstruction by hygromatous transformation of the lymphatics may have been responsible for the chylothorax and chylopericardium. Both these conditions were produced in dogs by ligation of the superior vena cava above the azygos veins.[14] Obstruction of the lymphatics of the neck and mediastinum produced by ligation and obliteration with sodium morrhuate injection produced both chylothorax and chylopericardium in dogs.[15]

Prompt surgical excision of cervicomediastinal cystic hygromas is indicated. A concomitant chylopericardium should be suspected and, if present, treated by transthoracic ligation of the thoracic duct. In this case, in retrospect, the latter might possibly have been a lifesaving measure.

Summary

The incidence, pathogenesis, and treatment of cervicomediastinal cystic hygroma are presented. The case of an infant with massive hygromatous lesions of the cervical, axillary, subscapular, and mediastinal regions associated with chylopericardium, the second such case, is reported. Early surgical intervention, with ligation of the thoracic duct if chylopericardium is present, is recommended.

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Effect of Operation on Serum Transaminase Levels

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Since the first observations by LaDue and co-workers, in 1954, the serum glutamic-oxalacetic transaminase determination (SGO-T) has become a widely accepted adjuvant for the diagnosis of acute myocardial infarction.[1] It is of particular value when the clinical picture or electrocardiogram is atypical. Operative and postoperative cardiovascular crises produce situations that are atypical as a rule. History is usually unobtainable; examination often is difficult: leukocyte count, sedimentation rate, temperature, and other indices are distorted by the surgical procedure. The electrocardiogram is of inestimable value, but it has limitations: Diagnostic electrocardiographic changes may take time to develop; they may be obscured by ventricular arrhythmias or intraventricular block, and subendocardial lesions may cause only nonspecific changes. The clinician is not infrequently faced with the dilemma of an unresponsive, hypotensive patient whose electrocardiogram may show only sinus tachycardia and primary T-wave changes.

If the SGO-T determination is to be of value in assessing the possibility of myocardial infarction in such patients, the effects of various surgical procedures on SGO-T levels must be investigated. Certainly the trauma of operation, and possibly the effects of general anesthesia, would be expected to produce a transitory rise.[2] The purpose of this study was to gather such data. The number of cases investigated was small but adequate for statistical analysis.

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Methods

A total of 246 determinations were made on 54 patients, chosen at random. An attempt was made to include as many different types of operations as possible. None of the subjects showed any evidence of postoperative myocardial infarction, but a few developed other complications. Blood specimens were drawn peroperatively (in all but two instances) and at various intervals during the first 10 postoperative days (Table 1). Only cases with preoperative levels within the normal range were selected for statistical analysis; there were 46 of these. In our laboratory 8 to 40 units is considered normal and 40 to 50 units borderline.

The specimens were run in duplicate; when values did not match, the determinations were repeated. In the procedure used, the amount of oxalacetate formed by the action of SGO-T in one hour was determined colorimetrically by the formation of a "hydrazone," which is highly colored.*

Results

The individual determinations and other pertinent details are shown in Table 1. Statistical analysis of data from cases with preoperative SGO-T values within the normal range shows without question that a significant increase in serum levels can be expected in the majority of cases (Table 2). The values plotted in the accompanying Figure show a maximum increase on the second postoperative day and a return to the preoperative range by the seventh postoperative day. A significant elevation could be detected on specimens drawn immediately after the procedure in the postanesthetic recovery unit (PARU).

From the Figure, it can be seen that the over-all average rise from the preoperative measure was not large (15.5 to a maximum of 27.3 units on the second postoperative day). However, the magnitude of the rise

* Sigma Chemical Company, St. Louis.
A Beckman Model DU spectrophotometer at 505μm. was used for these determinations.

TABLE I.—*Preoperative and Postoperative Levels of Serum Glutamic Oxalacetic Transaminase*

Case No.	Operation	Pre-operations	PAH *	Postoperative Levels, Days										Findings
				1	2	3	4	5	6	7	8	9	10	
	General Surgery													
1	Cholecystectomy with common-duct exploration			9	32	20	15				14			
2	Hemorrhoidectomy	16	16		13				10					
3	Cholecystectomy with common-duct exploration	16		15		43				30				
4	Right colectomy and ileosigmoidostomy	21		18		12				20				Adenocarcinoma of colon with liver and omental metastases
5	Inguinal herniorrhaphy	10		8						25				
6	Diagnostic laparotomy; drainage of subphrenic abscess	22		76		66				46				Died 4 mo. later; postmortem diagnosis: hepatitis, tuberculous cystic disease of liver, choledochitis
7	Liver biopsy; common-duct exploration; duodenotomy	180			137									
8	Subtotal gastrectomy	12	30			70								Died on 4th postoperative day of acute hemorrhagic pancreatitis
9	Gastrostomy and liver and stomach biopsy	31			71	103						39		Portocaval shunt 1½ mo. later
10	Gastric antral excision of pancreas pseudocyst			30										Nine hr. of anesthesia
11	Anterior sigmoid resection	18		23		31								
12	Anterior sigmoid resection	24	41	59	38	38	47							6½ hr. of anesthesia
13	Left axillary mass biopsy	14	18		14	7	19							
14	Diaphragmatic herniorrhaphy; vagotomy; pyloroplasty	21		58	20	21	17	21						
15	Bilateral lumbar sympathectomy	18		28	38	37		21						Moderately advanced inactive tuberculosis; amputation right 4th toe 13th postoperative day
16	Inguinal herniorrhaphy	14	15	18	14	13	9	10						
17	Excision of lipoma, posterior cervical area	14	11	15	12	8	9							
18	Cholecystectomy	44	40	93	38	38	37	27					37	Chronic pancreatitis 1 mo. postoperatively 59 units; multiple intrahepatic calculi remaining
19	Cholecystectomy; common-duct exploration	72	52	41	29	33	25	36						
20	Excision of presacral neurolemnoma	40	42	29	17	14	8	10						
21	Left inguinal herniorrhaphy	17	14	32	29	25	20				19			Residual recent cerebral vascular accident
22	Right radical neck dissection and left supraomohyoid dissection	15	26	25	24	15			28	20				
23	Laparotomy for G. I. bleeding	15	37	20	23	16			16	13				
24	Split-thickness skin grafts to groins	10	9	23	14	17	9			7				

TABLE 1.—*Preoperative and Postoperative Levels of Serum Glutamic Oxalacetic Transaminase*—Continued

Case No.	Operation	Pre-operations	PARU [a]	Postoperative Levels, Days										Findings
				1	2	3	4	5	6	7	8	9	10	
25	Left parietal brain abscess: craniotomy and excision	17		31			20	21	21	21	24			Paraplegia resolved postoperatively
26	Decompressive laminectomy L-5	12		35		53				26				
27	Laminectomy L-5; adhesive arachnoiditis	19					20							41 units at 14 days postop. 1950, at 3½ mo. postop., with serum jaundice
28	Cervical laminectomy and iliac bone fusion	14		34										
						Orthopedic								
29	Left high amputation	11				43	41						17	Paraplegic T-12 hematoma in stump
30	Left tarsometatarsal arthrodesis	14		14		9				13				
31	Revision right below-the-knee stump and right patellectomy				11			9	14				17	
32	Biopsy TB abscess, left iliac fossa			18		10				13				
33	Debridement of feet (bone and granulations)	10		7		9				5				
34	Syme's amputation	16		18		32				18				Persistent drainage and pain requiring below the knee-amputation 1 mo. postop.
35	Left medial meniscectomy	18		29	18									
36	Pantalar arthrodesis	18		25	26									
37	Right acetabul-sequestrectomy	15		27										
38	Removal of screws, proximal right ulna	17		18		19								
39	Left hip disarticulation; rhabdomyosarcoma	16		23	38		31	57	114					Postoperative temperature of 101, with wound hematoma, persistent sinus tract for 6 wk.
40	Jewett nailing fixation, left hip	23	31	50	45	45	40			27				Multiple attempts at reduction in O. R.
41	Right knee arthrotomy for osteochondritis	7	10	18	20	15	11			9				
42	Local excision lipoma, left thigh	15			11									
						Urologic								
43	Transurethral resection of prostate (TURP)	7		10		14				13				
44	Right orchiectomy and epididymectomy; evacuation hematoma	13		13		20					9			
45	TURP and bilateral vasectomy	27		19							11			
46	TURP and bilateral vasectomy					18		26		15				
47	TURP	13		15		25								
48	TURP bladder neck	23			40	33	29	27	22					
49	TURP and bilateral vasectomy and circumcision	13			23		18				17			
50	First-stage Johansen			12		12	13							
51	Right nephrolithotomy	12		38		35								Urinary infection with fever and presistent wound drainage

TABLE 1.—*Preoperative and Postoperative Levels of Serum Glutamic Oxalacetic Transaminase*—Continued

52	TURP	43		39		46		72	72	Persistent fever and G. U. infection post-op.; 1½ mo. post-operative abdominal resection
					Thoracic Surgery					
53	Right total pneumonectomy			52		39				
54	Right apical and posterior segmentectomy	15	32	58	43	47	44	23		Tuberculosis

* PARU stands for postanesthesia recovery unit.

from preoperative measure to the measures from PARU, postoperative (day) 1, and postoperative (day) 2 was sufficiently large enough not to be accounted for by chance. In other words, a statistically significant rise did occur.

Considering the variability of measures at PARU, postoperative 1, and postoperative 2, it is possible to determine that only the most extreme postoperative response elevates serum levels of SGO-T to the range considered diagnostically significant for acute myocardial infarction. Extending the range of the postoperative 1 and 2 measures to +2 standard deviations reveals that there is less than one chance in a thousand that the operative procedures alone will cause a rise above 60 units (Figure).

The total picture is not nearly this simple, however, when individual cases are analyzed. The observations above would be grossly misleading if certain important exceptions were not kept clearly in mind.

TABLE 2.—*Statistical Analysis in Forty-Six Cases in Which Preoperative Transaminase Levels Were Normal*

	Preop.	PARU	Postop. 1	Postop. 2	Postop. 7
Mean	15.5	22.3	25.7	27.3	17.5
Standard deviation	5.27	11.0	13.9	14.5	4.97
Standard error	0.98	2.9	2.38	3.1	1.21
t		2.06	3.96	3.2	1.29
P		<0.05 *	<0.001 *	<0.005 *	0.20 *

* Difference between preoperative and present level.

Clinically significant elevations were found to occur under the following circumstances:

1. Liver biopsy, subphrenic abscess drainage, or other procedures involving manipulation of the liver (e. g., hiatus hernia repair), Cases 6, 7, 9, and 14

2. Biliary tract surgery, Cases 1, 3, 18, and 19

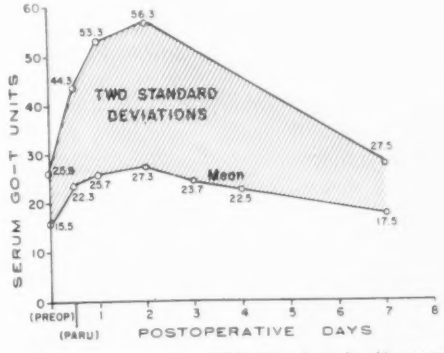
3. Procedures resulting in extensive trauma to skeletal muscle, Case 40

4. Postoperative complications, such as large abscesses or hematomas with cellular necrosis and hemolysis, Cases 8, 39, and 52

5. Thoracotomy with pulmonary resection, Cases 53 and 54

6. Elevated preoperative levels due to preexisting liver disease, biliary obstruction, or massive tissue necrosis, Cases 18 and 19

7. Possibly prolonged anesthesia (longer than five hours), Case 12



Mean postoperative SGO-T values in 46 cases showing normal preoperative levels. The shaded area denotes the range within 2 standard deviations from the mean. PARU refers to the time during which the patient was in the postanesthesia recovery unit.

These were the exceptions which could be identified in this small series of cases. Undoubtedly there will be others as experience widens.

Comment

Glutamic-oxalacetic transaminase has a differential concentration at the cellular level, being present in heart, skeletal muscle, brain, kidney, liver, testis, lung, and spleen, in decreasing order.[3] Cellular necrosis results in a postulated release of transaminase through the injured cell membrane with resultant elevation of the serum level. This hypothesis rests on the observation of decreased cellular transaminase in 90% to 98% of infarcted tissues.[4] The level of SGO-T activity following infarction has subsequently been proved experimentally and clinically to correlate with the degree of cellular injury, the amount of tissue necrosed, and the relative cellular concentrations of transaminase within the particular organ affected.[5] The last-mentioned factor becomes important when the amount of tissue necrosis required to cause an elevation of the SGO-T is taken into consideration. As little as 1 gm. of infarcted myocardium (as compared with an average total weight of 300 gm.) will raise the SGO-T above normal. In skeletal muscle considerably more necrosis is required for the same elevation. Hepatocellular disease or injury tends to involve the entire liver parenchyma. It is not surprising, therefore, that after injury to this large organ (1400 gm.) the highest recorded values of SGO-T are found. Clinically speaking, massive skeletal muscle injury or assayable liver malfunction usually becomes evident before a significant elevation in the SGO-T occurs.[2,6]

This is particularly true in tissues with even less concentration of transaminase and in the central nervous system, where there appears to be a blood-brain barrier. Large infarctions in brain or[2,6] pulmonary parenchyma are required to raise the serum transaminase. Case 26, involving surgical drainage of a large brain abscess, showed no elevation of SGO-T postoperatively. On the other hand, both cases of thoracotomy showed a moderate rise. Interestingly, similar observations have been made by Wroblewski and associates following thoracotomy in dogs.[4]

Comparison of mean values discloses that the maximum elevation following operative procedures occurs about 24 hours later than that resulting from acute myocardial infarction. The latter usually reaches a peak within 18 to 36 hours and is on the decline by the second day; the former continues to rise through the second day and gradually declines thereafter. From a practical standpoint this difference appears to be of no diagnostic importance.

Operative procedures should not, therefore, mask the effects of acute myocardial infarction on the SGO-T in the average patient. As is so often the case, however, the final decision as to whether a patient has sustained significant postoperative myocardial damage will depend on clinical judgment. The fact that, statistically, it would be very unlikely for operation alone to raise the serum transaminase above 60 units must be balanced in each individual case against the duration of anesthesia, the amount of trauma involved, and the type of procedure. More specifically, the exceptions previously referred to must be borne in mind.

Summary

There is a statistically significant rise in the level of serum glutamic-oxalacetic transaminase early in the postoperative period. The mean peak occurs on the second postoperative day. A fall to the preoperative value occurs by the seventh postoperative day. Statistically, there is less than one chance in one thousand that an uncomplicated operation will produce SGO-T values within the range that is diagnostic of acute myocardial infarction.

The exceptions in which abnormal elevations might occur included (1) biopsy or

manipulation of the liver, (2) biliary tract surgery, (3) extensive trauma to skeletal muscle, (4) large postoperative abscess or hematoma with cellular necrosis and hemolysis, (5) thoracotomy with pulmonary resection, and, (6) possibly, prolonged anesthesia.

If these exceptions are kept in mind, the SGO-T determination should be helpful in evaluating acute myocardial infarction during the postoperative period.

Dr. Richard L. Cutler, of the Department of Psychology, helped in the statistical analysis and interpretation of these data.

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The Terminolateral Anastomosis

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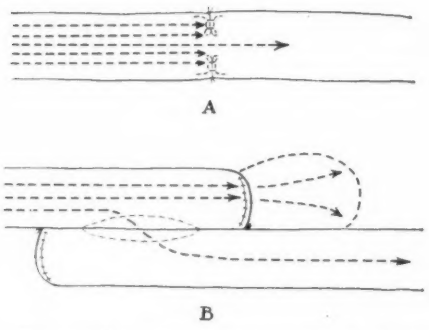

Fig. 1.—*A*, schematic representation of a diaphragm which might be turned in with an end-to-end anastomosis, impeding the normal passage of intestinal contents. *B*, schematic representation of side-to-side anastomosis with dilatation of the blind end.

Various types of bowel anastomosis have been described and used with satisfaction for many years. The end-to-end anastomosis is probably the most popular, but it has two distinct disadvantages. When the bowel lumen is small, it may be significantly narrowed by the diaphragm which is turned in (Fig. 1*A*). In addition, when there is significant disproportion between the approximated bowel ends, the unequal placement of sutures predisposes to leaking at the anastomosis.

The side-to-side anastomosis produces a large lumen with a relatively small diaphragm, but it has the disadvantage that dilatation of the blind end may occur (Fig. 1*B*). Furthermore, when there is marked disproportion between the bowel segments, dilatation of the larger one will sometimes compress the smaller, producing a temporary partial obstruction. However, our greatest objection to the side-to-side anastomosis is its inefficiency. It seems wasteful of time and energy to close one opening and then make another.

The end-to-side anastomosis has some of the undesirable features of both the end-to-end and the side-to-side anastomosis.

The anastomosis described here, which we have elected to call terminolateral, combines the more desirable features of the others and has none of their disadvantages. The inverted diaphragm is small in proportion to the size of the lumen; the existing orifices are utilized, and there is no blind end. Furthermore, the lateral incisions can be made so that the circumferences of the two segments of bowel are always equal.

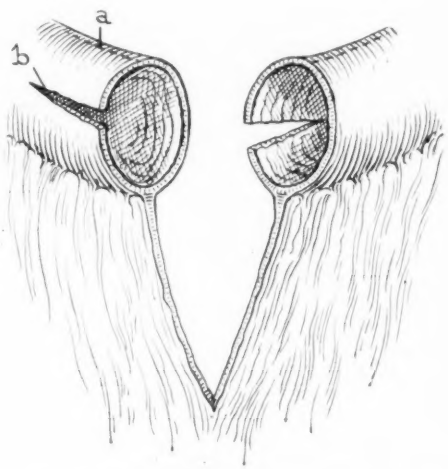

Fig. 2.—Drawing to show location of slit on the side of both the proximal and the distal loop. (*a*) represents the antimesenteric border, and (*b*) represents a position about midway between the mesenteric and the antimesenteric border. The slits are made sufficiently long to permit one to produce the size of lumen desired and to make the circumference of the two loops equal.

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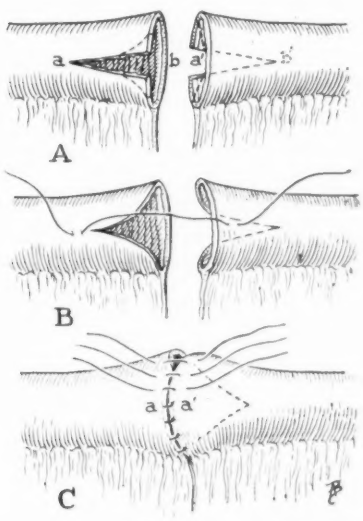

Fig. 3.—Drawing to show the placement of sutures in the anastomosis.

During the past five years we have utilized this anastomosis with increasing frequency and have recognized no disadvantages. The bowel to be anastomosed is prepared as usual. If the bowel lumina are equal and adequate, an end-to-end anastomosis is preferred. If the bowel lumina are unequal, the bowel with the smaller lumen is slit down the side until the two circumferences are equal. This slit is always made midway between the mesenteric and the antimesenteric border, and we have never had difficulty with the blood supply to the upper side. If the two orifices are small, both segments of bowel are slit until the circumferences are equal and adequate (Fig. 2). We round off the corners of the lateral slit, and the anastomosis is completed in the usual manner (Fig. 3). An added advantage of this technique results from the fact that the two leaves of mesentery overlap and approximation is easily accomplished with a few sutures.

Cheatle, in 1897, described a similar procedure, but the slit was placed on the antimesenteric border. When this technique is used, there is a tendency for the two leaves of mesentery to be angled apart. Poth,[2] in 1950, published an article demonstrating the procedure illustrated here. Formerly, a common application of the terminolateral anastomosis was the closure of a double-barreled colostomy following obstructive resection. When one crushed the colostomy spur, in the process of closing such a colostomy, a terminolateral anastomosis was performed.

We have found the procedure especially useful in performing ileocolostomy, after right hemicolectomy, and for the esophagoileostomy of right-colon esophagoplasty.[3]

Summary

The terminolateral anastomosis results in a large lumen with a small diaphragm. It utilizes the existing orifices and permits the approximation of bowel segments of equal circumferences. It results in an overlap of the mesentery, which facilitates closure of this defect. We think it deserves wider adoption.

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Anomalous Pulmonary Venous Drainage

The Successful Surgical Treatment of Total Anomalous Pulmonary Venous Drainage from the Left Lung to the Coronary Sinus

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In our experience, anomalous pulmonary venous drainage associated with interatrial septal defects has been common. Of 100 patients operated on under direct vision for interatrial septal defect, 17 have had associated abnormal pulmonary venous drainage. Of these 17 cases, 15 had anomalous drainage from the right lung and 2 from the left lung. The 15 cases with anomalous drainage from the right lung can be further classified: 5 cases had anomalous drainage from the entire right lung into the right auricle; 7 cases had only partial anomalous drainage into the right auricle, while 3 cases had anomalous drainage into both right auricle and superior vena cava. In one case the anomalous drainage from the left lung was entirely into the coronary sinus; in the other it was into the right auricle.

Usually, we have found that anomalous venous drainage of the right lung entered the right atrium just to the right of a secundum-type defect. The closure of the defect, with the resulting transposition of the anomalous venous drainage into the left atrium, required the relatively simple maneuver of closing the anterior aspect of the defect to the atrial wall lateral to the anomalous openings. In the case to be reported, however, there was total anomalous venous drainage of the left lung directly into a dilated coronary sinus associated with a patent foramen ovale. There was no left superior vena cava.

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The development of this anomaly is clarified by briefly reviewing the embryology of the pulmonary venous system.

According to Butler,[1] initially one finds routes of venous drainage of the lung into the venous primordium that develop into the superior vena cava, innominate veins, coronary sinus, proximal portion of the subclavian veins, portal vein, gastric veins, ductus venosus, and inferior vena cava. However, the permanent and normal connections of the lungs to the heart depend on regression of these initial temporary connections and development of secondary connections between the heart and the capillary plexus of the developing lungs. One can see, if the initial temporary venous connections persist, that many variations of anomalous pulmonary venous drainage may occur.

Clinically, the sites of termination of anomalous pulmonary veins, in order of their descending frequency,[2-4] are the superior vena cava, the ring atrium, the left innominate vein, and occasionally the coronary sinus, inferior vena cava, azygos vein, left subclavian vein, portal vein, and ductus venosus.

In our unusual case, we were faced with the problem of directing the coronary sinus, which contained oxygenated blood from the left lung and venous blood from the heart into the left atrium. The technical aspects of this repair and the physiological significance of the transplantation of the coronary sinus into the left atrium, we feel, are of such interest as to warrant this report.

Report of a Case

A 9-month-old boy was admitted to Colorado General Hospital for the second time on July 11,

1956, because of a heart murmur and cyanosis which had been present since birth. He had previously been hospitalized in April, 1956, because of a thrill and murmur, and at that time the diagnosis was in doubt. Since that time the child had gained weight poorly, had been extremely irritable, and developmentally was retarded. Physical examination revealed the patient to be a slightly cyanotic, thin, poorly nourished white male infant. The heart was found to be enlarged by percussion to the anterior axillary line. There was a Grade 4 systolic murmur over the entire precordium and back, with maximum intensity in the region of the left nipple. There was also a Grade 2, soft, blowing middiastolic murmur heard along the left sternal border. The second pulmonic sound was split and widely reduplicated. There was no evidence of clubbing or edema, and the peripheral pulses were full. The electrocardiogram showed right atrial and right ventricular hypertrophy. A chest x-ray revealed the pulmonary vascularity to be markedly increased. The aorta was inconspicuous. The hemoglobin was reported as 12.0 gm. %.

On July 16 the patient was taken to the cardiopulmonary laboratory for cardiac catheterization. The results of this study revealed the venous blood from the vena cava to be markedly depleted of oxygen, having saturations from 26% to 30%. Blood oxygen saturation jumped significantly in the right atrium, being 80% at the midatrial level. The pulmonary flow was found to be two and one-half times the systemic flow. Pulmonary artery pressure was elevated to 55/3. Brachial artery saturation was 75.8%. From the above data, evidence was obtained for the shunting of blood from both right to left and left to right. These shunts were through an interatrial septal defect. In view of the patient's poor course, surgical correction was advised.

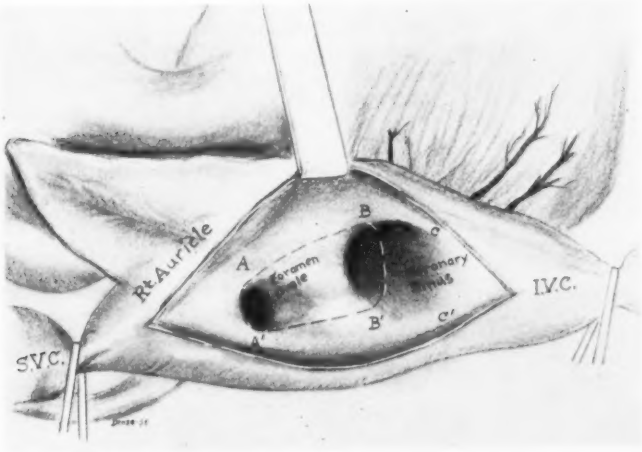
On Aug. 13, under general hypothermia, a bilateral fourth interspace transternal thoracotomy was done. Following inflow and outflow occlusion, the right atrium was opened, and a small atrial septal defect, apparently a patent foramen ovale, approximately 1 cm. in diameter, was found. Medial and inferior to this defect was a second large opening, measuring approximately 3 cm. in diameter, which proved to be the dilated coronary sinus. It was possible to pass a Kelly clamp out into the left pulmonary veins through this opening. A search was made for a left superior vena cava, and none was found. No other left pulmonary veins could be found except those entering the coronary sinus.

Because of the short length and inaccessible position of the left main pulmonary vein, it was decided to attempt to transplant the coronary sinus into the left atrium. This was done by removing a rather large segment of the atrial septum and closing the medial edge of the defect and coronary sinus to the atrial wall. The complicated operation appeared at the end to have been technically successful. The findings at surgery and surgical repair are described in the Figure.

The child had an uneventful postoperative course and was discharged on the 10th postoperative day.

Two months following discharge, repeat cardiac catheterization revealed no evidence of either a right-to-left or a left-to-right shunt, and the pulmonary artery pressure had fallen to 38/3. Brachial arterial oxygen saturation was 100%.

The child was last seen in clinic on July 10, 1957. It was noted that since his last visit he had gained weight well. He sat alone and walked without support. There was no clubbing, cyanosis,



Operative diagram of the defect and the surgical procedure. The atrial septum and the superior wall of the coronary sinus were excised along the dotted line. Closure is indicated by the letters, *A* being sutured to *A'*, etc., thus transposing coronary sinus to left auricle.

or edema. The heart did not appear enlarged. On auscultation no murmurs were heard.

Comment

The first case of anomalous pulmonary venous drainage was reported by Winslow in 1739.[5] It was not until 1902 that Nabarro[6] reported anomalous pulmonary drainage into the coronary sinus, as in the case here reported. It remained for Kirklin[7] to report in 1953 the first entirely successful repair of anomalous venous drainage from the entire left lung to the left innominate vein by anastomosis of the left pulmonary vein to the left atrium.

Our encounters with anomalous pulmonary venous drainage had been limited mainly to the type wherein the pulmonary veins from the right lung entered the right atrium just superior to an I-A defect and posed no particular problem for correction. However, in the case here reported, we were confronted with the problem of how much of a right-to-left shunt would result from transplanting the coronary sinus into the left atrium.

By placing the coronary sinus in the left atrium, approximately 100 cc/min. of unsaturated blood is presumed to enter the left atrium. This is in contrast to approximately 900 cc/min. of saturated blood emptying into that chamber from the pulmonary veins. The preoperative catheterization data showed a peripheral saturation of 75%, which jumped to 100% in the same brachial artery postoperatively. Thus we can say that the coronary sinus blood entering the left atrium in this patient caused an undetectable right-to-left shunt.

Summary

An unusual pulmonary venous anomaly with an associated interatrial septal defect was successfully corrected surgically. A small right-to-left shunt created at the time of surgery proved to be physiologically insignificant.

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Chloroform Instillation of Common Bile Duct

Its Problems, with Report of an Immediate Untoward Reaction

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A case is presented of a residual common duct stone removed by chloroform instillation and biliary flush, with a discussion of the problem and the report of an unexpected reaction.

Report of a Case

A 25-year-old white housewife had had two episodes of right upper quadrant abdominal pain with radiation to the right posterior lumbar area during the past two years. The condition was diagnosed as gallbladder infection and was relieved each time with meperidine (Demerol) and penicillin injections.

Five weeks before admission she had colicky pain in the right subscapular area. Three weeks later, she was slightly jaundiced, and x-rays showed a nonfunctioning gallbladder. Pain radiated to the right upper quadrant of the abdomen and persisted in the back. Occurrence of this pain was unrelated to intake of fatty foods.

Eight days before admission she had icteric sclerae and dark urine. Six days later the stools became clay-colored. Although her appetite was regarded as unimpaired, she lost 15 lb. during the three weeks prior to admission.

The patient's father and uncle died of pulmonary tuberculosis. The uncle also had cirrhosis of the liver. There was nothing contributory in the personal history.

On admission, physical examination revealed a fairly well-developed and well-nourished, jaundiced, afebrile patient. The liver was smooth and firm; its edge was 4 cm. below the right costal margin. The right upper quadrant and the right costovertebral areas were tender. Thymol turbidity was 4.4 units; alkaline phosphatase 6.19 Bessey-Lowy units; total bilirubin (Van den Bergh) 12 mg. %; direct fraction 5.8 mg. %; indirect fraction 6.2 mg. %. The blood count, blood urea nitrogen, prothrombin, and bleeding and clotting times were normal. Cephalin flocculation test and abdominal and chest films were negative. Urine bilirubin was 4+ and urobilinogen 4+. The diagnosis was subacute cholecystitis with cholelithiasis.

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Course.—The symptoms persisted. The urine urobilinogen varied from 2 to 6.8 Ehrlich units in a two-hour specimen. Feces were slightly to strongly positive for urobilin and urobilinogen and negative for occult blood.

On the seventh day after admission a cholecystectomy was done, with exploration of the common bile duct and insertion of a single-lumen T-tube. Subacute cholecystitis was found, with cholelithiasis and marked lymphadenopathy around the common bile duct. Exploration revealed no demonstrable calculus in the common duct.

The patient had an afebrile, uneventful course. On the eighth postoperative day there was some right subcostal discomfort. Total bilirubin (Van den Bergh) was 2.9 mg. %; direct fraction 1.4 mg. %; indirect fraction 1.5 mg. %.

A choledochogram on the 10th postoperative day demonstrated a common duct calculus, causing almost complete obstruction adjacent to the ampulla of Vater (Fig. 1). The calculi removed at operation were found to be easily fragmented by heated chloroform in vitro. To ensure adequate

Fig. 1.—Choledochogram on the 10th postoperative day.

liver protein preparatory to chloroform instillation, the patient was placed on a high-protein, low-fat diet.[1]

On the 12th postoperative day, total proteins were 8.2 gm. %; A/G ratio 4.3/3.9; Alkaline phosphatase 9.2 units; total bilirubin (Van den Bergh) 1.83 mg. %; direct fraction 0.65 mg. %; indirect 1.18 mg. %. Thymol turbidity 2 units; cephalin flocculation negative. Amylase was normal.

On the 15th postoperative day, the biliary flush regimen and heated chloroform T-tube instillation, according to Best,[2] were started. A modified polyethylene tube (Fig. 2) was easily threaded into the long arm of the T-tube up to the junction of the short arms. The pinhole was directed toward the ampulla or the inferior arm. With the patient sitting up, the chloroform was introduced into the polyethylene tube. Except for feeling of warmth, there was no clinically manifested untoward effect.

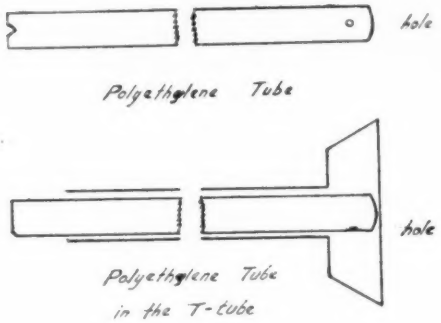

Fig. 2.—Modified polyethylene tube inserted into single-lumen T-tube for introduction of chloroform.

On the second day of the chloroform instillation, the patient felt warm, became unresponsive, and suddenly fainted. The blood pressure was 100/78; the pulse, 90 a minute, regular, and strong, and the respiratory rate 28 a minute and of regular rate and depth. Her color was good, and her pupils were 5 mm. in diameter and reacted equally and normally to light. The room was well ventilated. Hyperventilation was carried out with the oxygen mask; after three minutes the patient awoke as from a deep slumber and said: "I guess I fell asleep." She was normally responsive then, without any complaint. That night she had anorexia, nausea, and loose bowel movements.

The patient experienced pain and nausea when ether was slowly instilled into the choledochus the succeeding day.

On the second and third days, to-and-fro instillations of a given amount of saline or chloroform could not be carried out as readily as on the first day.

Fig. 3.—Choledochogram two days after chloroform instillation.

Thereafter the T-tube was clamped the whole day without any symptoms. The appetite improved. Two days later choledochograms showed no further evidence of calculus in the biliary tree (Fig. 3).

Four days after the chloroform instillation regimen, the total protein was 7.1 gm. %, with the A/G ratio 3.9/3.2, total bilirubin (Van den Bergh) 1.9 mg. %, direct fraction 0.3 mg. %, indirect

Fig. 4.—Choledochogram two weeks after chloroform instillation.

Fig. 5.—Intravenous cholangiogram eight months after chloroform instillation.

fraction 1.6 mg. %. Alkaline phosphatase 10.2 units; thymol turbidity 1.9 units; cephalin flocculation 2+; amylase normal. She was discharged two days later with prescription for a synthetic choleretic.

Two weeks later, the cholecholangrams (Fig. 4) were normal, the alkaline phosphatase was normal, and transaminase was 65 units. She had no clinical jaundice and had gained 12 lb. The T-tube was removed.

Eight months later intravenous cholangiograms were normal (Fig. 5). She was well, asymptomatic, and had gained 35 lb.

Comment

Pribram[3] has estimated the incidence of residual common duct stones to be 15% to 25% of operations for choledocholithiasis. Common duct calculi were found by Best[4] to be intrahepatic in origin in 7% of cases. Small stones may dislodge into the common duct during operative manipulation of the gallbladder. The commonest source of the residual stone, however, is the calculus overlooked at the first operation.[5]

Various ways have been used to detect this overlooked stone. Among these are the operative cholangiogram and the common duct explorations. The first was reported by experienced surgeons not to be technically satisfactory in 5% to 15% of cases and was proved to be inaccurate in 10% of cases. Johnston and associates[6] felt that the number of stones overlooked after manual exploration of the common duct (8%) compared favorably with the number overlooked using operative cholangiograms.

Reoperation for removal of a residual stone is not particularly welcomed by the patient. It is unsatisfactory in a patient of poor operative risk. The mortality rate for surgical removal of impacted stones in the ampulla ranges from 20% to 40%, and the operation is not necessarily successful.[7] In Hicken's study of 110 cases, 75% required reoperation for removal of common duct stones. Twelve of these (14.5%) had three or more explorations.[8]

Nonoperative means for removal of residual common duct stones have been tried by various authors. Different solvents have been used to dissolve or fragment the stones. Drugs such as atropine, glyceryl trinitrate (nitroglycerin) and topical dibucaine (Nupercaine) have been utilized to relax the sphincter of Oddi. To flush out debris or calculi in the biliary ducts, a regimen of biliary flush was introduced by Best.[5]

Pribram, following his method of introducing ether through a T-tube, reported success in 51 cases.[3] Using a mixture of ethyl ether and ethyl alcohol, fragmentation and expulsion of common duct stones was achieved by Walters and Wesson.[9] Narat and Cipolla[10] used 5 cc. of heated chloroform to soften stones during the surgical operation. Others have tried solution G (a solution of citric acid, magnesium oxide, and sodium carbonate), lauric acid, and dog and ox bile.

Best, Rasmussen, and Wilson[2] evaluated 113 agents and found only ether and chloroform to be satisfactory as biliary calculus solvents. Warm chloroform, heated to 61 C, is more effective. They recommended the concurrent use of a three-day biliary

flush regimen with relaxant drugs for the sphincter, thus bringing all the helpful factors to play in removing the stone.

A tube inserted in the common duct at the time of operation is a requisite for instillation of calculus solvent into the duct. Pribram cited use of the single-lumen T-tube to account for the failure of the ether method in other hands.[3] The tube allows the ether to evaporate upward into the liver, instead of reaching the stone. He advocated the use of a single tube, preferably of double lumen. It will direct the flow of ether toward the stone and make removal of the tube easier, with less trauma.

Strickler and associates[11] passed a ureteral catheter down the T-tube under fluoroscopy to place satisfactorily the tip near the stone. The double-lumen 135 degree-angled T-tube described and used by Best[12] has decided advantages.

In our case the popular single-lumen T-tube was used. Knowing the advantage of directing the flow of solvent primarily toward the stone, a polyethylene tube was modified to attain that result, instead of inserting a ureteral catheter down the T-tube under fluoroscopy.

Polyethylene tubing, smaller in diameter than the T-tube, was sealed at one end with a flame. At one side of the tube about 2 mm. from the closed, smoothed-out end, a 1 mm. pinhole was made. A mark was placed at the other end of the tube to indicate on which side the pinhole was located. The polyethylene tube was inserted easily into the lumen of the long arm of the T-tube up to the T-tube junction. Then the pinhole and the mark were directed toward the site of the stone, in this case toward the ampulla. Injection of the solvent through this tube directed the solution to the stones and away from the liver. The small hole created a jet-like spray, producing a turbulence which may have helped in the dissolution of the calculi,

To relieve spasm at the sphincter of Oddi, glyceryl trinitrate or atropine was used. Singleton and Coleman[13] noted in some cases that a dibucaine solution formed a heavy white precipitate when mixed with bile.

Warm chloroform (61 C) was used, as recommended by Best, not only because it is a better solvent but also because it is heavier than bile and tends to settle down, thus coming in contact with the stone in a less diluted state.

On the second day less of the instilled chloroform could be aspirated for the to-and-fro agitation than on the first day. Apparently, most of the 5 cc. of chloroform instilled the second day passed out of the common duct into the duodenum. Within two or three minutes the patient became unconscious and could not be awakened by voice or shaking. The cardiorespiratory status was clinically within normal. She remained in this state about two minutes. Oxygen was administered with a mask. In less than three minutes she regained consciousness, awakening as from a deep slumber, without any apparent untoward symptom or sign.

During the instillation of the solvent the patient was placed in a semirecumbent position, in order to place the heavier-than-bile chloroform mostly around the stone located at the ampulla. Nitrite syncope was ruled out because the patient did not have glyceryl trinitrate that day. The instilled chloroform, having passed suddenly into the duodenum and been absorbed in the blood, could very well have anesthetized this patient, just as chloroform is absorbed into the vessels of the lungs by inhalation. It was calculated that 18 minims (approximately 1.06 cc.) of chloroform is the average amount in the system of an adult required to cause insensibility.[14] Thus, only 1 cc. of the instilled 5 cc. of chloroform need to have been absorbed through the small intestine to render this patient unconscious. This disturbing reaction might indicate indirectly the release of the obstruction at the ampulla. Literature on common duct instillation of chloroform has not mentioned this reaction, which is hereby called to our attention.

Summary

A case of successful removal of a residual common duct stone using chloroform T-tube instillation and biliary flush is presented.

A modified polyethylene tube inserted into the single-lumen T-tube will facilitate the introduction of a solvent.

Chloroform instilled into the common bile duct could possibly make the patient unconscious by being absorbed through the blood vessels of the small intestine.

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Carcinoma of the Intrahepatic Bile Ducts

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The surgical therapy of carcinoma of the biliary tract is fraught with difficulties. The proximity of the biliary tree to the hepatic blood supply has long presented a formidable barrier to successful extirpation. Carcinoma of the extrahepatic biliary tree may usually be seen and felt during exploratory surgery, and, although the pathological features of these tumors often vary considerably from the commonly accepted conception of malignancy,[1] the obstruction to bile flow usually is obvious and proper measures are instituted.

When the tumor arises from the intrahepatic part of the bile ducts, and thus is not directly accessible to visualization and palpation, the problem of detection is added. The armamentarium available to the physician for establishing the diagnosis of obstructive, or surgical, versus parenchymatous, or medical, jaundice before operation is formidable but far from specific. Diverse conditions of the liver not amenable to surgery may present the same signs and symptoms as mechanical obstruction to the main bile ducts, and sometimes the burden of proof is left to the surgeon to establish by exploratory laparotomy the true nature of the disease. The three cases presented here illustrate some of the problems of detection and diagnosis of intrahepatic obstruction to the bile ducts and what results may be obtained by palliative therapy.

Report of Cases

CASE 1.—A 56-year-old man entered the hospital on March 18, 1956, with the chief complaint of cirrhosis of the liver. Eight months prior to admission he began to feel poorly and lost his appetite and 40 lb. in weight. His urine became dark and the stools light; the skin felt itchy, and one day his friends remarked that his eyes were yellow. Six months prior to admission he underwent an abdominal exploration in another hospital, and the diagnosis of biliary cirrhosis was made on liver biopsy. The jaundice persisted, but he felt better after the operation and gained weight. Lately the patient again felt poorly, and became listless, with anorexia and malaise.

Physical Examination.—The patient was well developed but showed signs of weight loss and was deeply jaundiced. The liver could be palpated 4 fingerbreadths below the right costal margin and was slightly tender.

Laboratory Examination.—Urine 4+ reaction for bile. Alkaline phosphatase 94.4 units. Bilirubin 47.1 mg. %, direct fraction 28.8 mg. %, indirect fraction 18.3 mg. %. Sulfobromophthalein (BSP) retention 64.3%. Prothrombin time 20.0 seconds; control 13.2 seconds. There was no blood in the stools.

Operation (March 30, 1956).—The liver was greatly enlarged, smooth, and yellow-brown. Exploration of the abdominal organs, including the gallbladder and common duct, revealed that these were of normal size but did not contain bile. Exploration was carried on into the hilus of the liver, and 2 cm. above the junction of the hepatic and cystic ducts the common hepatic duct felt hard and firm to palpation. Aspiration with a needle did not reveal any bile. A needle was plunged into the hilus of the liver, and a bile-containing cavity was encountered 3-4 cm. above the thickened area of the duct. The hepatic duct was opened and found to contain firm, reddish nodular tissue, which grossly had the appearance of carcinoma. Frozen section did not reveal any tumor tissue. A polyethylene catheter was forced up the hepatic duct into the cavity discovered before. A cholangiogram revealed this to be the right hepatic duct (Fig. 1). The left hepatic duct could not be identified. A T-tube was placed with one arm in the right hepatic duct and the abdomen closed.

A paraffin histological section was made of the biopsy material and the diagnosis of carcinoma established (Fig. 4).

Postoperative Course.—The patient recovered well. A cholangiogram one week after operation showed diminution in size of the right hepatic duct

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Fig. 1 (Case 1).—Cholangiogram, March 30, 1956. Dilated right hepatic duct and branches.

(Fig. 2). The jaundice disappeared, and the stools became brown. The patient was discharged one month after operation with the T-tube clamped. After discharge he had a few episodes of chills and fever. Arrangements were made for terminal care. Six months after operation the patient felt well; he was gaining weight. One year after operation the patient felt "wonderful." He had gained 40 lb. in weight and was employed at light work. The T-tube was irrigated every week and returned golden bile. A cholangiogram 14 months after operation showed normal right hepatic duct branches (Fig. 3). Two years after the operation he complained of occasional nosebleeds. Soon after this he was admitted because of melena. The site of origin was not determined, and the patient was discharged after receiving transfusions.

Comment.—This patient has survived in relative comfort two years since his operation and almost three years since the onset of symptoms. The correct diagnosis was not made at the first operation, possibly because of insufficient exploration. No attempt was made to remove the tumor because of its location, but the prolongation of life amply justifies the efforts made to establish an internal biliary fistula.

Case 2.—A 71-year-old man entered the hospital on Oct. 9, 1957, with jaundice, painless, of three months' duration. There had been some episodes of fever and a weight loss of 15 lb.

Physical Examination.—The patient was a thin, well-developed, jaundiced man. The liver was palpable 3 fingerbreadths below the right costal margin. There were no other abnormal findings.

Laboratory Examination.—Urine contained no bile. Urobilinogen positive in 1:256 dilution. On duodenal drainage, no bile was obtained. Serum bilirubin 3.2 mg. %; direct reacting fraction 1.6 mg. %; alkaline phosphatase 13.6 units; thymol turbidity 2 units; cephalin flocculation 2. There was no occult blood in the stools.

Operation (Oct. 17, 1957).—The liver was enlarged. The gallbladder and common duct were of

Fig. 2 (Case 1).—Cholangiogram, April 9, 1956. Only the right hepatic duct and part of the gallbladder are filled. There is marked decrease in the size of the bile ducts.

normal size. Exploration of the hilus of the liver revealed a thickening around the right hepatic duct. The main hepatic duct was opened and a probe inserted into the right hepatic duct, where an induration was felt but no stones. A cholangiogram (Fig. 5) revealed obstruction of the right hepatic duct. Tissues could not be obtained inside the duct for biopsy, so that dissection was carried farther externally, and in the substance of the liver around the duct a hard mass was discovered; a biopsy specimen was taken, which revealed carcinoma (Fig. 6).

A T-tube was placed in the common duct and a catheter inserted into the left hepatic duct.

Postoperative Course.—The patient did well postoperatively. The T-tube was irrigated once every week and free flow of bile obtained. The jaundice disappeared, and he was discharged on the 14th postoperative day. Six months after surgery the patient was feeling well; he had gained 24 lb. in weight. There was no return of the jaundice.

Comment.—Strictures of the bile ducts are known to be caused both by neoplastic growth and by benign scar formation.[1] Strictures of the intrahepatic bile ducts have been reported with increasing frequency[2] and, in the absence of histological proof of malignancy, have been classified under the term benign sclerosing cholangitis. A well-known characteristic of the bile ducts, both in experimental animals[3] and in human beings, is to react to injury with excessive outgrowth of fibrous connective tissue. Occasionally the initial damaging agent may be completely overshadowed by this protective reaction. A recent publication drew attention to the fact and produced evidence that in previously diagnosed cases of sclerosing cholangitis true carcinomatous neoplasms might sometimes exist. The anatomy of the intrahepatic ducts provides an opportunity for growths of this kind to go undiagnosed for a long time. The sacculi, or vasa aberrantia, which sometimes are referred to as mucous glands, branch throughout the fibromuscular coat of the ducts and may extend and communicate outside its wall.[10] A carcinoma arising in the extra-

Fig. 3 (Case 1).—Cholangiogram, July 5, 1957. There is filling of the branches of the right hepatic duct. The caliber is normal.

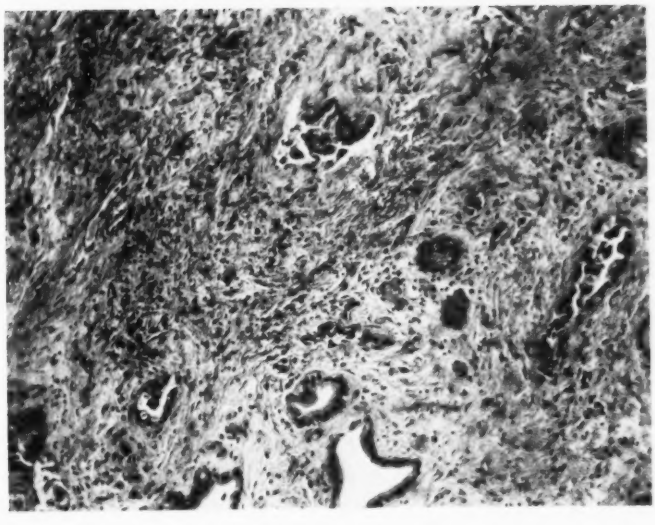

Fig. 4 (Case 1).—Biopsy tissue taken at operation. In the lower part of the picture there are normal-looking sacculi, or mucous glands. In the upper half there is attempted gland formation by tumor cells. Hematoxylin-eosin stain; reduced to 80% of mag. ×150.

Fig. 5 (Case 2).—Cholangiogram during operation. Only the left hepatic duct is outlined.

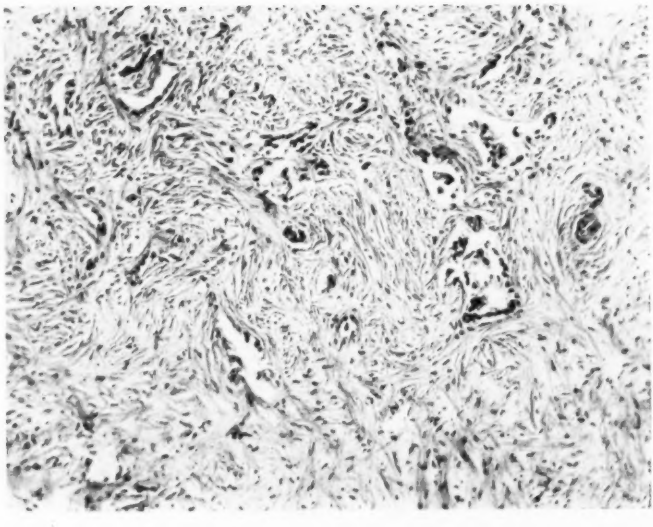

Fig. 6 (Case 2).—Biopsy tissue from outside the right hepatic duct. The lesion can be recognized as a scirrhous carcinoma.

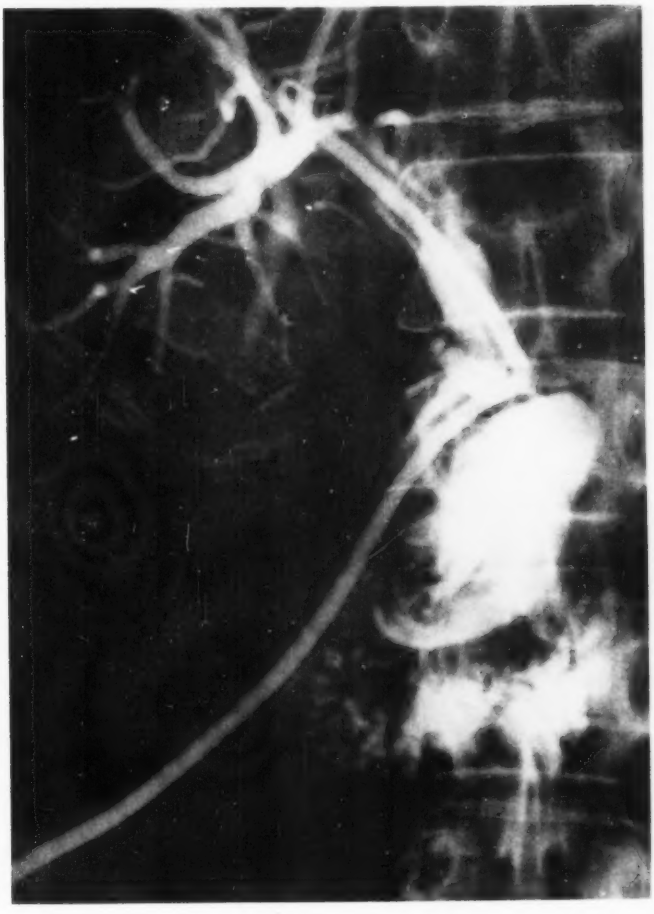

Fig. 7 (Case 3).—Cholangiogram during operation, Aug. 30, 1955. Only the right hepatic duct is visualized.

luminal locations will still be a true neoplasm of the bile duct, but may present itself as a stricture caused by the compressing action of fibrous tissue proliferation. The accurate diagnosis of such lesions may be quite difficult, as removal of biopsy tissue from the inside of the duct may not reach the tumor. Biopsy of the mass outside the duct often shows only fibrous tissue, and occasionally the tumor may be so well differentiated that diagnosis of malignant tumor is impossible from a small specimen.

CASE 3.—A 55-year-old woman was first seen in the outpatient clinic in March, 1955. She complained of attacks of severe right upper quadrant pain, radiating to the right scapular region. The patient's mother had died of carcinoma of the liver. Gallbladder roentgenograms showed a normally functioning gallbladder without stones. There was no jaundice, but alkaline phosphatase was elevated to 15 units. Although the patient had had recurrent symptoms for over a year, she refused the recommended operation. Six months later, after continued symptoms of pain and questionable attacks of jaundice, she consented to surgery and was admitted.

Physical Examination.—The patient was well developed and well nourished. There was no evidence of jaundice on physical examination, and no abdominal masses could be palpated.

Laboratory Examination.—The gallbladder now failed to visualize on the Graham-Cole test. An intravenous cholangiogram also failed to show the gallbladder, but the common duct was visualized and was possibly dilated. Alkaline phosphatase was 21 units; serum bilirubin 1.7 mg. %; sulfobromo-

Fig. 8 (Case 3).—Cholangiogram, Aug. 30, 1956. The cholangiogram looks similar to that taken the year before.

phthalein retention 31.2%. Thymol turbidity 1 unit; cephalin flocculation 1; cholesterol 336 mg. %, and protein 8.2 gm. % with a 5.7/2.5 albumin-globulin ratio. The stools did not contain occult blood.

Operation (Aug. 30, 1955).—The liver was slightly enlarged. There was a hard tumor nodule in the right lobe of the liver. The gallbladder was of normal size and contained no stones. The common duct was somewhat dilated. A choledochotomy was performed, and from the lower end of the common duct a fleshy piece of tissue was extracted. A frozen section revealed this to be carcinoma (Fig. 10). Probing of the hepatic ducts revealed the right one to be patent, but the left was filled with firm tissue. A cholangiogram verified obstruction of the left hepatic duct (Fig. 7). Some of the tissue was scooped out of the left hepatic duct and on microscopic examination was found to be of the same character as the loose part of the tumor removed from the common duct. A biopsy specimen of the tumor nodule on the surface of the liver was also taken (Fig. 11).

A T-tube was placed in the common duct, with the long arm in the right hepatic duct.

Postoperative Course.—The patient recovered promptly from surgery. She has been followed since in the outpatient department. The T-tube is in place and is irrigated once a week. It is now over two and a half years since the operation. The patient is working full time, feels well, and is asymptomatic.

Comment.—Occlusion of one hepatic duct is well compatible with life.[9] Acute occlusion of one hepatic duct is not followed by jaundice if the liver is not too diseased, but there is a prompt rise in alkaline phosphatase.[9] Jaundice in this case occurred

Fig. 9 (Case 3).—Cholangiogram, March 11, 1958. There is poor filling of the radicles of the right hepatic duct.

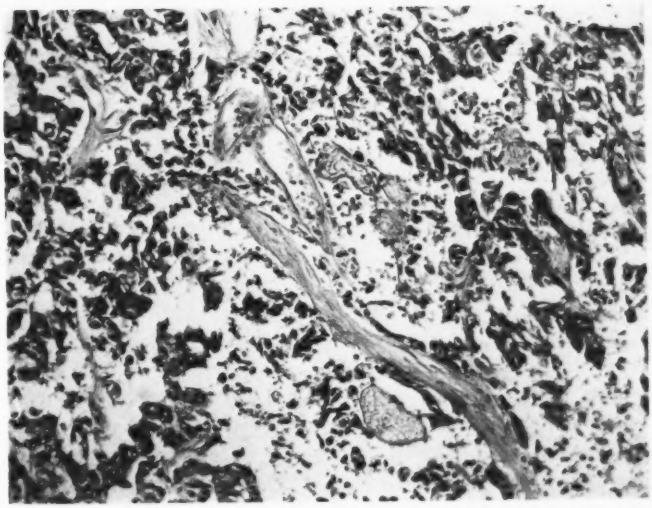

Fig. 10 (Case 3).—Piece of tumor tissue removed from common duct at operation. Hematoxylin-eosin stain; reduced to 80% of mag. × 150.

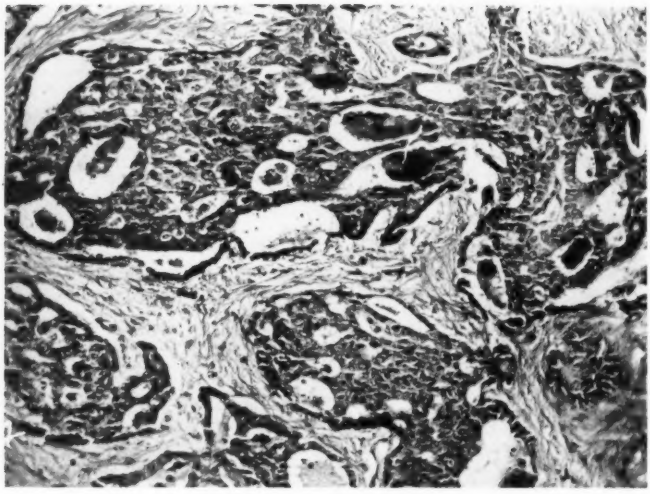

Fig. 11 (Case 3).—Biopsy specimen from liver metastasis at operation. As in Figure 10, the appearance is one of intraductal papillary carcinoma. Hematoxylin-eosin stain; reduced to 80% of mag. ×150.

only when a piece of the tumor from the left hepatic duct migrated into the common duct and thus compromised total biliary flow. Cholangiograms (Figs. 7 and 9) taken since operation show patency of the right hepatic duct, but on the last one there may be an indication of narrowing, presumably on the basis of extension of the tumor.

General Comment

Malignant tumors of the bile ducts have been known for their poor prognosis. The survival, after diagnosis has been made, is usually measured in days, rather than in weeks or months.[4] Often the proper diagnosis is not made at operation [5] because of the confusing appearance presented by these lesions.[1] The excessive fibrous reaction in relation to the tumor mass has also been noted in earlier reports.[6,7] References are also made to the frequently small size of the tumors, which cause early death by biliary obstruction,[1,6] and to the fact that the majority of the patients are without evidence of metastases.[5] For the group of tumors located in the intrahepatic part of the bile ducts in particular, the problems of detection and histological diagnosis are emphasized. The death of these patients occurs from liver failure in various forms. Evidence is produced here to show that if drainage of bile is afforded from some part of the liver, life in comfort may be prolonged over a considerable length of time. It is well known that the human being needs only a small part of functioning liver to ensure homeostasis. Cases are on record in which obliteration of one or the other of the hepatic ducts has occurred from operative trauma and the patient has survived without jaundice.[8] In animals, up to 75% of the hepatic ducts have been ligated without causing jaundice,[9] and benign tumors of the left hepatic duct have caused obstruction to the outflow from that lobe without evidence of liver insufficiency or jaundice.[11] The right hepatic duct has been deliberately ligated in a human being with cirrhosis, and no measurable increase in jaundice has occurred. There is thus evidence that jaundice and liver failure do not supervene until the growth in one hepatic duct extends over on the common hepatic duct and thus obstructs the outflow from both lobes. The tumors in this location have been shown to spread along the portal spaces and thus to compress and obliterate the ducts before serious involvement of the liver parenchyma occurs. The insertion of a splint to prevent occlusion of the

duct will allow continued drainage of bile internally and thus prolong life and comfort until a later stage of the disease. The slow progress of the intrahepatic bile duct carcinomas recorded here and elsewhere[7] emphasizes the danger of assigning a benign nature to intrahepatic obstructing lesions on clinical grounds alone. Without the aid of adequate biopsy, which most of the time it is difficult to obtain, the possibility of an underlying carcinoma cannot be ruled out.

Summary

Carcinomas of the bile ducts are usually small lesions and cause death by obstructing the common channel from the liver.

Only a small part of the liver is necessary to prolong life in comfort if internal biliary drainage can be provided.

Carcinomas of the intrahepatic bile duct are slow-growing tumors and, because of difficulty in obtaining histological proof, may sometimes be mistaken for benign strictures.

Three cases of intrahepatic bile duct carcinoma are presented, in which patients have liver asymptomatic for a long period after simple T-tube drainage of one lobe of the liver.

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Primary Carcinoma of the Gallbladder

An Analysis of Fifty-Two Cases

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A statistical review of cases, in general, is attended with little difficulty, and the author, after completing a series, is usually contented with his findings. But it is indeed a difficult matter when one attempts to make a study of malignant diseases of the gallbladder, liver, and biliary tract. This is due primarily to the final diagnosis, placed upon the chart and recorded in the record room, many of the cases being tabulated from a clinical angle, often without waiting for the receipt of a final microscopic examination; others bearing a different microscopic interpretation on the part of the pathologist.

Four hundred eighty-eight case histories have been reviewed; all have been classified under "malignant disease of the gallbladder, liver, and biliary tract." Of these, 52 cases of primary carcinoma of the gallbladder have been noted, 48 appearing in the Albany Hospital between the years 1935 and 1957, inclusive, and 4 from the Veterans' Administration Hospital, Albany, N. Y., between the years 1952 and 1957, inclusive. Sixteen cases were so questionable as not to warrant tabulation.

There were 58,105 patients (exclusive of the specialties) admitted on the surgical service of the Albany Hospital between the years 1935 and 1957, inclusive. Of these there were 3692 cases of diseases of the gallbladder, liver, and biliary tract; of these, there were 124 cases of primary malignancy, 48 of which were of primary carcinoma of the gallbladder.

Surgical statistics, on the whole, may be misleading, owing to unsatisfactory explorations, and to many cases of surgical inoperability. Only those cases proved by microscopic examination, from tissue removed either at operation or at autopsy, were considered worthy of tabulation.

This review was made primarily to evaluate our cases from the standpoints of (1) incidence of calculi, (2) pathology, (3) chief complaints and signs and symptoms, (4) radiography, (5) types of operations performed, (6) treatment, and (7) morbidity and mortality rates, based upon as complete a "follow-up" as was possible.

A discussion of the etiologic possibilities and a complete review of the literature are presented in brief form only. The study is based especially upon the findings, as a result of meticulous analysis.

Analysis of Cases

1. *Incidence of Calculi.*—Authors differ somewhat as to the incidence of calculous gallbladder and primary carcinoma of the gallbladder. The proportion may vary with different clinics, from 1% to a high of about 10%. Of 488 cases of malignancy of the biliary tract in the Albany Hospital, from 1936 to 1957, inclusive, primary carcinoma of the gallbladder was present in 9.8%.

A close relationship between the presence of calculi and carcinoma of the gallbladder has been recognized for many years, and all agree that calculi may enter into the picture of the malignant disease as, at least, a predisposing factor. Arminski,[2] in an exhaustive report of 2067 cases, showed that 73.2% of patients presented calculi. To this series may be added the reports of Mohardt,[23] 85%; Lam,[19] 87%, and Lichten-

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stein,[20] 69.3%. Our series showed an incidence of 80.7%.

Ewing[12] believed that a combination of factors determines the formation of this disease, namely, mechanical irritation by the calculi, inflammatory conditions, exciting hyperplasia, cholesterol metabolism, and the irritative action of the bile.

Arminski[2] cited Aschoff and Lancereau, who believed that calculi either formed in the cancerous gallbladder or were merely coincidental findings, and that calculi were formed secondary to the carcinoma.

On the other hand, Roberts[28] cited Comfort and co-workers, who stated that of 112 patients with asymptomatic gallstones, who were followed for at least 10 years, none developed carcinoma of the gallbladder. In the same report, Roberts cited Donald and Fitts, who reported 100 patients having cholecystostomy without cholecystectomy and stated that none of those patients developed primary carcinoma of the gallbladder.

Basing his report on experimentation with cats, Fortner[15] concluded that there is a possibility that cancer of the biliary tract is caused by a carcinogen in the bile, since this finding showed that five out of six cats that had received a single pellet of methylcholanthrene in the lumen of the gallbladder developed primary carcinoma of the gallbladder with invasion of adjacent organs and with metastases. These animals survived from 23 to 32 months. Fortner agreed that the compound which he used was chemically related to the naturally occurring substances in the bile.

Rivkin[27] supported this theory, stating that the chemical composition of some calculi is in many cases similar to that of known carcinogens and expressed the belief that the irritant may act directly on the undifferentiated basal layer of the epithelium, which is continuously producing new epithelium.

Burrows[8] reported that when foreign bodies were introduced into the gallbladders of 50 guinea pigs, which had subsequently survived for periods of 9 to 359 weeks, there was no instance in which cancer of the gallbladder had developed. Be that as it may, we must agree with the remark of Evarts Graham[17] that "stones should be considered as being a definite precancerous lesion." This conclusion is agreed upon by the vast majority of experienced surgeons. That calculi are an obvious source of mechanical irritation, supplemented perhaps by a carcinogenic factor in the bile, must be a rational conclusion.

2. *Pathology.*—The microscopic pathology of the gallbladder is dependent upon (1) the location of origin, (2) the type of tumor present, (3) the progress of the disease, (4) complications, such as empyema, etc., (5) the presence of surrounding tissue invasion, distorting its configuration, and (6) the location of calculi. Indeed, the neoplasm might be entirely overlooked by experienced surgeons at the time of operation. The gallbladder may be large and distended, or contracted, thickened, and indurated, or it may appear normal at the time of operation. In the scirrhous type of carcinoma, the gallbladder is generally contracted, hard, rather irregular, and small, whereas in the colloid and mucinous types it is distended, with, as a rule, thin walls and at times ulcerations. It is this type of tumor that is found especially in conjunction with a calculus about the cystic duct or with diseased tissue about that area. Perforation occurs especially in the colloid or mucinous type. With the presence of polyps, the gallbladder is likely to be distended. When empyema or hydrops is present, the organ will be distended, perhaps to a marked degree. Ewing quoted Kaufmann, who stated that "after the stomach, the gall-bladder is the most frequent source of gelatinous carcinoma of the peritoneum."

Adenocarcinoma, with its variations, is most commonly found. In our series, the incidence was 71.1%, with the desmoplastic form 5.7%, colloid form 3.8%, papillary form 11.5%, scirrhous form 1.9%, and cyst adenocarcinoma 1.9%. In this series, three adenocarcinomas presented polyps with ma-

TABLE 1.—*Histologic Classification*

Adenocarcinoma	20
Colloid or mucinous	4
Desmoplastic	3
Papillary (3 with polyps)	6
Anaplastic	7
Melanocarcinoma	1
Squamous-cell carcinoma	5
	52

Cirrhosis present in 4 cases.

lignant changes and one was benign (Table 1).

Of the anaplastic type, the percentage was 11.5; the incidence of the squamous-cell type was 9.6%; 5.7% were diagnosed only as carcinoma and 1.9% as melanocarcinoma.

Biliary cirrhosis was present in 7.6%; chronic cholecystitis, in 3.5%; acute cholecystitis, in 4.5%, and empyema, in 1.9%. Perforation was present in 1.9% and a sinus tract in 3.6%. The gallbladder was distended in 60.7% and contracted in 39.2%.

Metastases and Extension: Metastases or extension to the liver is common; when one considers the anatomy of the lymphatic channels about this organ, the cystic nodes at the junction of the cystic and common ducts, the lymph nodes about the liver, and the lymph nodes about the head of the pancreas, one would naturally expect these pathways of drainage to form a natural path for extension and metastases. Distant metastases are fairly rare but do occur, as shown in Tables 2 and 3.

TABLE 2.—*Metastases and Extension of Primary Gallbladder Carcinoma*

	Ext.	Metast.		Ext.	Metast.
Liver	16	16	Peritoneum	6	
Cystic duct	4		Omentum	3	
Common bile duct	4		Pancreas	2	2
Hepatic duct	2		Vertebrae	2	
Portal vein	1		Sigmoid	2	
Hepatic vein	1		Mesocolon	2	
Periaortic l. n.	2		Fallopian tube	1	
Celiac l. n.	3		Ovary	4	
Mesentery l. n.	3		Uterus	1	
Mediastinal l. n.	1		Duodenum	1	
Regional l. n.	8		Bladder	1	
Diaphragm	1		Peripancreatic l. n.	2	
Lung	5		Abdominal wall	1	
Adrenal	1		G. I. tract	1	

No metastases or extension 14.

Metastases from distant sites of origin to the gallbladder were found more frequently than is commonly supposed (Table 3).

3. Chief Complaints and Signs and Symptoms.—Abdominal pain, usually in the right upper abdominal quadrant, was found in the vast majority of the cases, though a few presented no pain at all. Jaundice followed very closely. Following in order were "gallbladder attacks," nausea, vomiting, indigestion, etc.

The duration of illness varied from a few years to a few hours—the symptoms were present a few weeks in the major portion of our cases. Rarely, in our series, was the duration one of years. This disease is usually so insidious as to exhibit a most bizarre symptom-sign complex. As noted by many, it may present, in its early stages, all the evidences of a benign biliary disease, accompanied by cholelithiasis. Too often, the clinical picture will represent that of a metastatic lesion far from the gallbladder, and hence the primary site will be overlooked in arriving at a definitive diagnosis. The laboratory helps us but little. All authors are well agreed as to the predominating signs and symptoms. In our series, the clinical picture was of the usual type. Anorexia and anemia were rarely present unless the disease had progressed to an extreme degree.

TABLE 3.—*Primary Site of Metastases to Gallbladder*

Lymphosarcoma	2	Hepatoma	1
Leukemia	1	Colon and hepatic flexure	1
Hodgkins disease	1	Sigmoid	2
Mesothelioma	1	Rectum	1
Melanoma (face)	1	Cecum	1
Body of uterus	4	Esophagus	1
Cervix of uterus	2	Ovary	9
Stomach	9	Prostate	2
Pancreas	5	Kidney	1
Liver, hepatic cells	1	Submaxillary gland	1
Liver, bile ducts	1	Breast	6
Bronchus	6	Hepatic duct	1

TABLE 4.—*Operative Procedures*

Cholecystectomy	7
With choledochostomy	6
With rt. hemicolectomy, biopsy of liver	1
With choledochostomy and hepaticocholecystostomy	1
With biopsy of lymph nodes	3
With gastroenterostomy	2
Partial cholecystectomy	2
With choledochostomy	1
With gastrojejunostomy, biopsy of liver	1
Cholecystostomy	3
With biopsy of gallbladder	1
With colostomy	1
With biopsy of gallbladder, choledochostomy & hepatic drainage	1
Biopsy of gallbladder, rt. hemicolectomy, ileocolostomy	1
Choledochostomy, choledochojejunostomy	1
Choledochostomy, with cecostomy	1
Biopsy of omentum	1
Biopsy of liver	4
Cecostomy	1
Questionable	4
No operation	9

4. *Radiography.*—It was interesting to note that a filling defect in the gallbladder was usually present, but there were negative findings for calculus in 30 cases in which calculi were present, as found at operation or autopsy.

5. *Types of Operations Performed.*—These procedures, in general, are cholecystectomy with or without drainage; drainage of the common bile duct and hepatic duct; block dissection, including gallbladder, lymph nodes, and contiguous tissue, with or without partial lobectomy, or partial hepatectomy.

6. *Treatment.*—I believe that treatment should be divided into three categories: (1) preventive, (2) palliative with the establishment of drainage, and (3) radical excision.

Preventive Treatment: Assuming that calculi are important etiologic factors, and certainly they are, we must consider that cholecystectomy, including cholelithotomy, is indicated. This approach is supported by most of the experienced surgeons. Finney [13] stated that "silent stones" is a deceiving term; Sainburg [30] said that an asymptomatic calculous gallbladder should be removed "on these grounds alone"; Graham [17] asserted that "stones should be considered as being a definite precancerous lesion"; Glenn [16] stated: "Prophylactic cholecystectomy for all patients in the older age group with symptomatic biliary tract disease can be justified on the basis of the dangers of malignancy. This procedure appears to be the most reasonable line of approach to the problem." Petrov [25] believed that "the desirability of prophylactic cholecystectomy for gallstones, in elderly women, receives experimental support." Childs [9] endorsed "prophylactic cholecystectomy for the asymptomatic calculous gallbladder." Finney [13] endorsed the line of treatment by stating that "With present day methods, prophylactic removal of an asymptomatic calculous gallbladder is entirely justified, unless there are complications." Benjamin [3] went so far as to say: "The only hope of reduction of the general incidence lies in early removal of a calculous gall bladder." Many other experienced surgeons support this view. On the other hand, there are many surgeons whose experience is unquestioned, and who take a less enthusiastic view of the above approach.

Palliative Treatment: The establishment of drainage may under certain conditions prolong the life of the patient, but probably for only a short time, and give him some relief from jaundice, nausea, and vomiting, and perhaps pain.

Radical Excision: An evaluation: When one considers the expediency of this line of procedure, due consideration must be placed upon the tendency toward rapid extension or dissemination throughout the lobes of the liver and extrahepatic ducts. Ackerman's [1] excellent description of the lymphatics of the gallbladder should be included in this report:

> The lymphatics of the gallbladder arise from the mucosa, travel through the muscular wall to empty into a subserous lymphatic network. The trunks empty into the lymph nodes of the anterior border of the foramen of Winslow, in the lymph node of the neck of the gallbladder and in the hepatic lymph node. These lymphatics have abundant anastamoses with the lymphatics of the liver.

As Burdett [7] concludes: "Dissemination of cells [occurs] not only in the liver but in regional lymphatics and beyond before the patient comes to operation."

Blalock's [4] statement, in 1924, that "in malignancy of the gallbladder, when a diagnosis can be made without exploration, no operation should be performed, inasmuch as it only shortens the patient's life" has been quoted by many authors. This concept has been challenged by some surgeons of today, and the approach to treatment has been of a most radical nature, including excision of mass, including the gallbladder, portions of the liver and regional lymph nodes, and, at times, resection of neighboring organs and total lobectomy.

In a review of the more recent literature, we find that Pack,[24] Rivkin,[27] Fish,[14] Sheinfeld,[32] Thorek,[36] Strohl,[33] Suma,[34] and Burdette [7] feel that at times radical procedure is warranted.

Pack,[24] advocating total lobectomy, appears to be the most optimistic as regards radical procedure.

Now, in analyzing the reports of these surgeons, it is quite important to note that these same authors and others are loath to give too bright a prospect to this form of treatment.

Strohl [33] is of the opinion that "extensive resection will not greatly improve the survival rate." Burdette [7] states that "radical surgery has not yielded encouraging results and has increased the mortality at operation." Rivkin [27] notes that "in the vast majority of cases, it is palliative and of little avail." Sawyer [31] emphasizes the fact that "results were unimpressive." Glenn [16] states that there is "small prospect of eminent substantial improvement in the prognosis of this disease, attributable to radical surgery." Roberts [28] believes that "partial hepatectomy along with cholecystectomy has not materially altered the end results."

On the other hand, Pack et al.[24] comment that "advanced cancers are usually inoperable by general standards, though possibly not through the medium of total lobectomy." Booher and Pack [5] conclude that, "despite marked anaplasia and regional node metastases, cancer of the gallbladder is a curable disease and an attempt to control this cancer is always in order."

All agree that wide excision of the liver should be performed rather than the so-called "wedge excision." On the other hand, there are those who have reported cases in which long survivals have followed simple cholecystectomy; these cases are, however, few. The reader is referred to the cases of Danzis,[10] Burdette,[7] Childs,[9] Rivkin,[27] Booher and Pack.[5] Marshall and O'Donnell,[21] in a recent report, however, noted 15 patients who had cholecystectomy as a primary procedure, and the average survival rate was seven months.

In our series, no partial or total lobectomy was performed.

7. *Morbidity and Mortality Rate.*—Operative: Nine patients died within 1 to 7 days; 13, within 2 to 4 weeks; 5, within 2 to 4 months; 9, within 5 to 12 months; 3 in 13, 15, and 19 months, respectively, and 1 died within 6 years following radical mastectomy for carcinoma of the breast with cerebral involvement.

Nonoperative: Nine patients died within a few months.

Survival: One survived 16 years, with melanocarcinoma; 1 was alive at 24 months, with no record of death (Bureau of Vital Statistics), and 1, at 41 months, with no record of death (Bureau of Vital Statistics).

Postoperative Complications: One died of coronary occlusion; one, of acute cardiac infarct; one, of pulmonary embolism; one, through accident, causing cerebral hemorrhage, and one, of subphrenic abscess.

Diagnosis.—Malignancy is to be suspected when the gallbladder presents thick, ulcerative or friable walls, especially in those cases in which there have been repeated attacks of biliary colic with or without calculi (especially the latter). It is these cases that demand preliminary frozen section.

There are loss of weight, anorexia, pain of a constant or boring nature, and malaise out of all proportion to that of recurring cholecystitis. There may be anemia, but it is surprising that in many cases the hemoglobin and hematocrit were normal, or even above normal.

Symptoms were frequently associated with cholecystitis and cholelithiasis. Once the tumor is symptomatic, it is nearly always incurable.

Unexpected Findings: The literature is replete with cases that were not diagnosed at operation and were recognized only by microscopic examination. Delannoy [11] reported that 5 out of 17 cases were undiagnosed at operation, and Rivkin,[27] that 4 were undiagnosed; Danzis [10] reported that in 44% the diagnosis was not made even at operation. Glenn [16] stated that seven cases were unrecognized at primary procedures, and Burdette [7] and many others emphasized the point that every gallbladder should be examined in the operating room; frozen sections are of paramount importance. In our series of 52 cases, 3 were unrecognized at operation.

Summary

Calculi were present in 80.7% of our cases, exclusive of seven cases in which inoperability was such as to preclude the recognition of their presence had such been the case.

There was no definitive symptom-sign complex, these findings corresponding with those of other observers.

Laboratory criteria were of no aid in diagnosing the condition; clinically, adenocarcinoma, with its varied forms, was the predominating pathologic finding.

Extension and metastases were commonly found in the liver, regional lymph nodes, and, to a less extent, the peritoneum and lungs, practically all of the organs being occasionally involved. Metastases to the gallbladder from the stomach, bronchi, ovary, and heart were not uncommon.

Females predominated (61.3%), while males represented 38.6%.

The decade with most frequent involvement was that from 61-70 years.

Radiographically, it was noted that of the 33 cases with calculi, only 3 showed shadows. This may possibly be an indication that a carcinogenic factor in the bile acts upon the calculi in such a way as to cause absence of the usual shadow.

It is imperative that frozen sections be made of the gallbladder in all cases in which the gallbladder is hard, thickened, or indurated. This dictum is substantiated by the fact that the literature shows abundant cases in which the diagnosis was not made, even at the operating table. This occurred in 3 of our cases.

A review of the recent literature shows that cholecystectomy with or without drainage of the biliary passages is of no avail in cure, though exceptional cases noted in this report indicate that very occasionally longevity is prolonged over several years.

In evaluating radical procedures, it has been noted that the great majority of surgeons feel that, of radical procedures, the so-called "wedge" excision of the liver is obsolete and that a goodly portion of the liver must be removed.

We are approaching the dictum that partial or complete lobectomy should be employed if the case presents any promising aspects. Even those who suggest these procedures are loath to give an optimistic view.

Too short a time has elapsed to permit a final judgment on those cases in which so far the results have been good. The prognosis is most discouraging, but the radical procedure of partial or total lobectomy should be considered as a recognized operation, and the modern surgeon must evaluate for himself the feasibility of such a procedure.

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Bronchogenic Carcinoma

Importance of the Cell Type

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Introduction

A greater number of cases of bronchogenic carcinoma are seen today than in the past. Whether this increase in frequency is real, or only seeming, is not definitely known, but more important is the fact that this disease presents a serious problem and is now relatively common. It is, therefore, imperative that all factors affecting treatment and prognosis be thoroughly evaluated. Although there have been many studies made and figures compiled of bronchogenic carcinoma, relatively few concerning the individual cell type have been reported. In the treatment of most tumors, one of the factors concerning the ultimate prognosis of the disease is its cell type. With bronchogenic carcinoma, however, the studies concerning individual cell types, although relatively few, have been largely controversial.

Many authors hold the view that the cell type is a highly valuable prognostic element.[1-6] Koletsky,[5] in 1938, in his correlation of the clinical course with the various cell types, concluded that there was a difference in the growth, spread, and prognosis of bronchogenic carcinoma and that this difference could be correlated definitely with the various cell types. Churchill,[6] in 1948, stated that, although it was reasonable to assume that tumors with poorly differentiated cells were rapidly invasive and that complete removal surgically was only a remote possibility, there had been no complete correlation of the postoperative prognosis and the cellular type. In 1951 McDonald and co-authors[3] presented an excellent study of the various cell types with regard to the ultimate prognosis, and they were of the opinion that the cell type had a definite bearing on the prognosis. Kirklin,[7] in 1955, in a similar study, concluded that the cell type was, without doubt, of important prognostic significance, and Paulson,[8] in 1957, stated that there was a close correlation between cell type and prognosis.

Contrary to these opinions, other authors have reported that the individual cell type has no prognostic significance.[9-12] Neuhof,[11] in 1948, reported that prognosis based on microscopic features could not be made with assurance and stated that the histologic features of bronchogenic carcinoma bore no significant relation to the postoperative prognosis. Similarly, a more recent work by Phillips[10] showed no correlation of prognosis with the type of tumor cell or location of the tumor within the lung.

Although at present there appears to be more evidence favoring a varied clinical course dependent on the different cell types, it is readily apparent that there is no complete agreement on this point. It is with this problem of correlating the clinicopathologic features of the various cell types that this study is concerned.

Methods and Materials

The clinical material was composed of all histologically proved cases of bronchogenic carcinoma treated at The Johns Hopkins Hospital during the 10-year period from 1942 through 1951. No patient after 1951 was included in order to ensure that all patients would have been followed at least five years. The histologic material from these

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patients was from either surgical or autopsy specimens. The clinical records were studied and the data recorded. Separately, and without knowledge of the clinical history, all histologic specimens were examined, and the cell type was determined. As far as could be ascertained, all cases in which there was another primary cancer were eliminated in order to prevent including metastatic tumors of the lung.

Letters requesting specific follow-up information were sent out on every patient who had not been heard from within the six-month period prior to this study. These letters, for the most part, were sent to the patient's physician and, occasionally, to the patient himself or his relatives, when the physician had lost contact with the patient. By this method the desired follow-up information was obtained.

Pathologic Study

During this 10-year period there were 351 histologically proved cases of bronchogenic carcinoma. Histologic diagnosis was made from tissue taken at thoracotomy alone in 126 cases. In 64 cases the diagnosis was made histologically at autopsy, and in 56 cases the diagnosis was made from material obtained at bronchoscopy. There were 43 cases diagnosed from lymph node biopsy and 5 from cell block study only. The remaining 57 cases were diagnosed by combinations of the above methods. Histologic material in some cases was limited to cytologic studies and bronchoscopic biopsies, both of which occasionally were inadequate to make a cell-type diagnosis, and no diagnosis other than bronchogenic carcinoma could be made. In other instances, even in resection cases, no diagnosis of cell type could be made with any degree of accuracy because of lack of a definite cellular pattern. These cases made up a group of 18 (5%). The remaining 333 cases (95%) were diagnosed as to distinct cell type.

Admittedly, it is difficult to classify various histologic patterns in any tumor, and, indeed, in many instances it is entirely unwarranted. One definitely should not try to force any tumor into a certain classification for the sole purpose of classification. There are many tumors which cannot be classified as to specific cell type with any degree of reliability, and continual subgrouping or subclassification adds nothing of value, serving only to make the issue more confusing and less accurate. Perhaps it is more accurate to speak of the "histologic pattern" of a tumor rather than of its "cell type," because a diagnosis can be made only on the basis of the cellular pattern in the entire tumor, and certainly not on a cytologic picture alone. In this study classification was made according to the predominant histologic pattern of the tumor, and there was no hesitancy in placing a tumor in the unclassified group if there was no definite cellular pattern. However, most tumors in this study (95%) were easily distinguishable as to a definitely predominant cell type. These cellular patterns are squamous-cell carcinoma, adenocarcinoma, and small-cell and large undifferentiated-cell types. This classification is the one used by Kirklin, McDonald, and co-authors[7] and is similar to the one set forth by Olcott.[13] It should be stated that a common classification in use is a somewhat simpler one, of three types—squamous-cell, adenocarcinoma, and undifferentiated-cell, the last including both the large- and the small-cell type. It was felt, however, after reviewing all the specimens in this study, that the small-cell carcinoma was a specific cell type and presented a characteristic histopathologic appearance, and therefore should be classified individually.

Eliminated from this study were alveolar-cell tumors and bronchial adenomas. The alveolar-cell tumor ("bronchiolar carcinoma," "adenomatosis," etc.) is usually distinguished by its characteristic histologic pattern, and there can be little doubt that this tumor forms a separate and distinct group, although there is much controversy as to its origin. Similarly, tumors of the bronchial adenoma group are of an entirely different nature from bronchogenic carcinoma and should occupy a separate classification. It is important to exclude these

tumors in any statistical study of bronchogenic carcinoma because of their entirely different behavior.

Incidence.—Of the 351 histologically proved cases, squamous-cell carcinoma was by far the commonest type, occurring in 150 patients (43%). The next most frequent was the large-cell type, present in 95 patients (27%), whereas there were 48 cases (14%) of the small-cell variety. Adenocarcinoma was present in 40 patients (11%), and in 18 cases (5%) no cellular type could be determined.

Squamous-Cell Carcinoma.—Squamous-cell carcinoma has a distinct histopathologic picture, and the diagnosis should be made only when there is evidence of epidermization; that is, the production of prickle cells, cornified epithelium, or keratin. The most differentiated tumors usually show multiple keratin pearl formation. Diagnosis based on a pattern of cells forming squamous-like sheets of infiltrating tumor is unwise because undifferentiated tumors often take on this appearance. Herein lies one of the major difficulties in evaluating varying reports of the incidence, treatment, and results of the squamous- and the large-cell type. The large, undifferentiated-cell carcinoma is often classified as "highly undifferentiated squamous carcinoma" or "anaplastic squamous carcinoma" and is thereby placed in the general group of squamous-cell carcinoma, when, in reality, there is no histologic evidence other than the general growth pattern for the squamous-cell classification.

Grossly, this tumor may occur anywhere along the bronchial tree but most commonly is situated in a central location, that is to say, in the main stem or lobar bronchus. In this study it was possible to determine accurately the gross location in all but 13%. The tumor was located centrally in 78% of the determinable cases, occurring in the main-stem bronchus in 13% and in the lobar bronchus in 65%. In 22% the tumor was in a peripheral position, that is to say, away from the lobar or main-stem bronchus (Fig. 1). Of the patients on whom

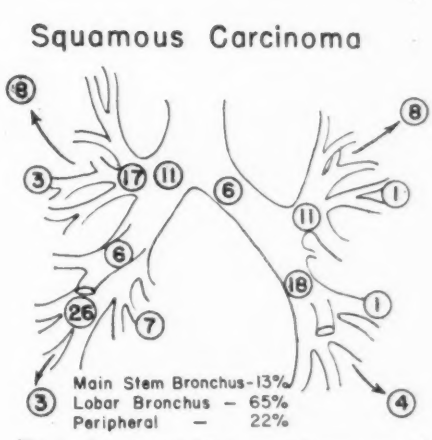

Fig. 1.—Location of 130 tumors of squamous-cell carcinoma type.

thoracotomy had been performed, tumor was present in the regional lymph nodes in 30%. The mediastinum was invaded by direct extension in 31%, and invasion of the pleura was present in 13%. Distant metastases were demonstrated in 14% of all patients when first seen.

Adenocarcinoma.—The histologic appearance of this type of tumor is that of a malignant tumor which consists of atypical glandular structures of varying sizes and shapes. These glandular structures may be papillary, acinar, or alveolar in arrangement and may or may not contain mucin. In some of the very poorly differentiated types mucin may be found intracellularly, thereby helping to make the diagnosis. In making a diagnosis of bronchogenic adenocarcinoma, metastatic adenocarcinoma should be ruled out. This procedure can be very difficult, and at times impossible, with the ultimate proof resting on the clinical course. Not infrequently squamous-cell carcinoma will form islands of cells with necrotic centers, which, at first glance, appear to be acinar in structure and can lead to an erroneous diagnosis if care is not taken. "Alveolar-cell" carcinoma and bronchial adenoma should be excluded, as already mentioned.

Grossly, the tumor more commonly occurs in the periphery approximately mid-

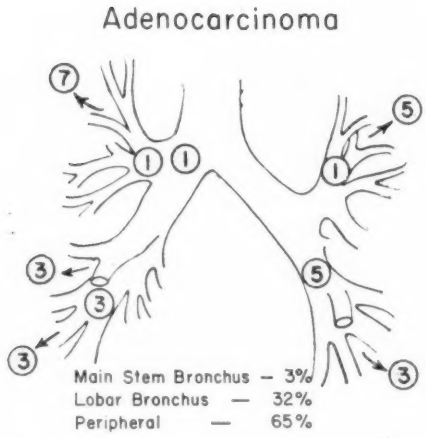

Fig. 2.—Location of 32 bronchogenic adenocarcinomas.

way between the hilus and the pleura. In early stages of the process there is considerable space between the tumor and the main-stem or lobar bronchus. Of the 80% of cases of this cell type in which the tumor was accurately located, it was located centrally in only 35%. In only 3% was the tumor in the main-stem bronchus, and the lobar bronchus was the site in 32%. The tumor was located peripherally in a significant 65% (Fig. 2). In the cases in which thoracotomy had been performed, regional lymph nodes were invaded in 33%, and direct extension into the mediastinum occurred in 38%. The pleura was invaded in a striking 58% of cases, a fact which was not surprising with the predominantly peripheral location of the tumor. Distant metastases were demonstrable in 20% of all the patients when first seen.

Small-Cell Carcinoma.—The distinct feature of this type is, of course, the small cellular component. The cells are about one and one-half to two times the size of a normal lymphocyte but are strikingly small in relation to other tumor cells. The cells are arranged in bundles or whorls and have a definite appearance, ranging from a distinctly spindle to a rounded shape, with very little cytoplasm and either a rounded or an elongated nucleus. Mitotic figures are numerous. The elongated type has frequently been given the name of "oat-cell carcinoma."

Grossly, this tumor arises, for the most part, in the main-stem bronchus and the subdivisions, and only rarely from a smaller bronchus. This is the most rapidly growing type and forms large masses, which both replace lung parenchyma and invade and encase the mediastinal structures, as well as the pleura. Another frequent occurrence is its rapid submucosal and submucosal-lymphatic spread, so that, although the bronchial mucosa may be intact, the bronchus itself may be entirely encased in tumor extending up and proximal to the carina. In 23% of the cases in this study the exact location of the tumor could not be determined accurately because of the massive growth. Of those that could be determined, tumor was located centrally in 76%, being present in the main-stem bronchus in 43% and in the lobar bronchus in 33%. It was located peripherally in only 24% (Fig. 3). In the patients operated on, tumor was present in the regional nodes in 45%, and direct extension into the mediastinum occurred in 60%. The pleura was invaded in 25%. Distant metastases were demonstrable in 23% of all the patients when first seen.

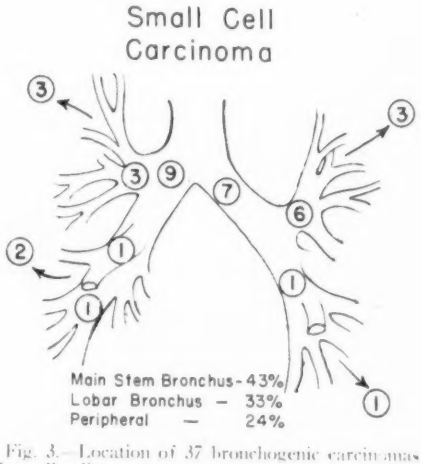

Fig. 3.—Location of 37 bronchogenic carcinomas of small-cell type.

Large-Cell Carcinoma.—Diagnosis of this cell type is largely a diagnosis by exclusion. There is no evidence of keratinization or epidermization, as seen in squamous-cell carcinoma, and there is no glandular formation or production of mucin, as seen in adenocarcinoma. Although all the cells are large, there is no definite pattern or arrangement of the cells, and this lack of any pattern is a characteristic feature. This tumor demonstrates the most bizarre growth of all and is composed of large polyhedral, rounded, or somewhat spindly cells in a loose syncytium with abundant cytoplasm. The nuclei, which are often very large, contain also very large nucleoli. Multinucleated tumor cells, along with distorted mitotic figures, are plentiful. There is absolutely no similarity to the small round-cell carcinoma.

Grossly, the tumor is predominantly located in a central position near the hilus. This tumor, like the small-cell type, tends to form very large masses, which invade the mediastinum and replace lung tissue, to invade the pleura and the chest wall. The exact location was not determinable in 24% of the cases. In the 76% in which it was determinable, the tumor was located centrally in 67%, with 18% in the main-stem bronchus and 49% in the lobar bronchus. Tumor was located peripherally in 33% (Fig. 4). In the cases in which thoracotomy had been done, regional lymph nodes were involved with tumor in 39%, and involvement of the mediastinum by direct extension occurred in 39%. The pleura was invaded in 14%. Of all the patients with this cell type when first seen, distant metastases were demonstrable in 27%.

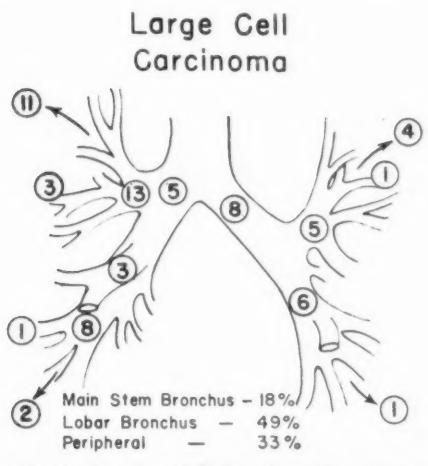

Fig. 4.—Location of 71 bronchogenic carcinomas of large undifferentiated-cell type.

Treatment

Of the 333 histologically typed cases out of the 351 in this study, 127 patients received no surgical therapy. Most of these patients had evidence of metastases and their tumors were clearly inoperable; but a few had other, unrelated conditions of such a severe nature that operative therapy was thought to be unwise, and a few patients refused surgical treatment. There were 200 patients who underwent thoracotomy, but only 107 had some type of resection. Therefore, although the operability rate was 62%, the resectability rate dropped to 32%.

There were striking differences in the ability to treat patients having the various cell types. There were 111 patients with squamous-cell carcinoma who underwent thoracotomy, and, of these, 71 had resectable tumor. This was an operability rate of 74% and a resectability rate of 47%. There were 11 palliative resections, and 60 resections were done with the idea of curing the patient. Of the 40 patients with adenocarcinoma, 16 had inoperable lesions. In the remaining 24 the tumors were operable but only 11 were resectable. Of these resections, 1 was palliative, and the other 10 were were done as a curative measure. This gives an operability rate of 60% and a resectability rate of 28%. Of the 95 patients with large-cell carcinoma, 44 had inoperable tumors. The remaining 51 tumors were operable, 23 being resectable. This was an operability rate of 54% and a resectability rate of 24%. Less than one-half of the patients with the small-cell type had operable carcinoma, only 20 out of 48

TABLE 1.—*Extent of Local Spread in 206 Patients at Time of Thoracotomy*

	Total Operable Cases	Hilar Node Invasion		Mediastinal Invasion		Pleural Invasion	
		No. of Cases	Per Cent	No. of Cases	Per Cent	No. of Cases	Per Cent
Squamous-cell	111	33	30	34	31	14	13
Adenocarcinoma	24	8	33	9	38	14	58
Large-cell	51	20	39	20	39	7	14
Small-cell	20	9	45	12	60	5	25
Combined	206	70	34	75	36	40	19

having had thoracotomy. Of these, only two had resections. This was an operability rate of 42% but a resectability rate of only 4%. Thus, at one extreme the squamous-cell type was resectable in 47%, whereas, at the other extreme, the small-cell type was resectable in only 4%. These data are summarized in Table 2. Of the patients with resections, the hilar lymph nodes contained tumor in these percentages: squamous-cell carcinoma, 27; small-cell carcinoma, 50; adenocarcinoma, 55, and large-cell carcinoma, 56.

Follow-up data on all patients in this study were complete in 95%, and there was a 99% follow-up of the patients who had had resection. There were 19 patients who survived five years or longer after resection. This is an over-all survival rate of 6% of all patients entering the hospital and a survival rate of 18% of all patients undergoing resection.

A breakdown of these figures according to cell types reveals differences in survival according to the cell type. Although resections could be carried out in two patients with the small-cell type, neither patient lived five years, both having died within five months of resection with recurrent carcinoma. This poor prognosis is usual in this type of neoplasm.[1,2,4] Of the patients with the large-cell type in whom resection was done, only one was living and free of carcinoma five years or more after resection. This is a survival rate of 4% of those with resection. One patient died 3 years 10 months after pneumonectomy of far-advanced pulmonary tuberculosis in the remaining lung; at the time of death there was no evidence of carcinoma. If this patient is included as cured, then the survival rate would be 8% of those with resection. There were two patients with adenocarcinoma who survived five years, but one patient died in the sixth year following resection, of generalized metastases. The other patient was free of tumor seven years following lobectomy but had a recurrence, which was resected. This patient has had no evidence of recurrence since that time, approximately one year prior to this report.

By far the best prognosis was in the squamous-cell type, as indicated by the fact that 16 patients, or 23% of those undergoing resection, survived five years or longer. Eleven of these patients are still alive, the longest survival in the group being 14 years. There was one patient who died in the sixth year following resection, of generalized me-

TABLE 2.—*Ability to Treat Patients with the Various Cell Types*

	Total No. Patients	Inoperable		Operable		Resectable	
		No. of Cases	Per Cent	No. of Cases	Per Cent	No. of Cases	Per Cent
Squamous-cell	150	39	26	111	74	71	47
Adenocarcinoma	40	16	40	24	60	11	28
Large-cell	95	44	46	51	54	23	24
Small-cell	48	28	58	20	42	2	4
All cases	333	127	38	206	62	107	32

TABLE 3.—*Number and Percentages of Patients Surviving Five Years or Longer, Following Resection, According to Cell Type*

	Total No. of Cases	Five-Year Survivors			
		No. of Cases	Per Cent of Cases Entering Hospital	Per Cent of Cases with Resection	Per Cent of Cases with Resection Leaving Hospital
All types	333	19	6	18	22
Squamous-cell	150	16 *	10	21	27
Adenocarcinoma	40	2 *	5	9	11
Large-cell	95	1	3	4	5
Small-cell	48	0	0	0	0

* One died in the sixth postoperative year of metastases and is not included in the percentages.

tastases. The other four patients all lived longer than five years and died of unrelated causes, being free of tumor at the time of death. One patient, not included in this group of 16 patients surviving five years, died of myocardial infarction two and a half years following resection, and had, at the time, no evidence of carcinoma. If the palliative resections are eliminated, then, of all patients undergoing resection with the idea of effecting a cure, 27% survived five years or longer. These data are summarized in Table 3.

Comment

It is obvious that information compiled from a group of patients having a tumor of a specific cell type cannot be directly applied to any one given patient with a tumor of the same cell type. The fact remains that in any given patient the factors of importance are the exact location of the tumor and to what extent and by what route spread has occurred. Therefore, to conclude that, because the patient has a particular type of tumor, his prognosis will be the same as that for the group is not sound. It can be stated, however, that the course of the various cell types tends to fall into a more or less definite pattern, which gives valuable information. Thus, in dealing with a patient having a small-round-cell carcinoma there is very little chance of effecting a permanent cure. In this group not a single patient was cured. On the other hand, in dealing with a patient having squamous-cell carcinoma, the chances are much more favorable, considering that 10% of all patients who entered the hospital with this type of cancer and 27% of those who left the hospital after resection survived five years or longer. Between these two extremes in prognoses are patients with adenocarcinoma and the large-cell type.

This fact does not mean that the patient with the small-cell type should not be operated upon if there are no surgical indications of inoperability; however, because of its location and rapid growth and spread, very few such tumors will be resectable at the time of operation. In this study, only 4% of all tumors of this type were resectable. These statistics do not indicate that the small-cell type of carcinoma having a favorable location should not be resected, but, rather, point out the fact that the chance of finding a favorable lesion in these cases is extremely small and that any heroic measure to attempt a cure in patients with this type of tumor is probably useless. On the other hand, not all patients with squamous-cell carcinoma will have a resectable tumor, but the chance of finding a favorable lesion is relatively good, since almost half the patients entering the hospital with this cell type of tumor were able to have resectional therapy. More of the patients with adenocarcinoma and the large-cell types of tumor will be cured than those with the small-cell type; however, even in these groups there is a considerably lower percentage surviving than in the group of patients with squamous-cell carcinoma. It would, therefore, appear that prognosis can-

not be founded on the cell type alone, but that the cell type is one important factor in the prognosis, since it determines to a large extent the location, rate of growth and spread, and therefore resectability and cure.

Summary

Of 351 histologically proved cases of bronchogenic carcinoma seen from 1942 to 1951 at The Johns Hopkins Hospital, 43% were of the squamous-cell, 27% of the large-cell, and 14% of the small-cell type; 11% were adenocarcinoma, and in 5% no cellular diagnosis could be made.

Squamous-cell carcinoma was found to be located principally in the lobar bronchus, to be the least extensive in spread, and to offer the best operability, resectability, and cure rates.

The small-cell type, at the other extreme, was located principally in the main-stem bronchus and was the most extensive in spread. This type had the lowest operability and resectability rates, and there were no cures.

Adenocarcinoma and the large-cell type had approximately the same operability, resectability, and cure rates. Adenocarcinoma was found principally in a peripheral location and had a definite tendency to invade the pleura and the chest wall. The large-cell type was located principally in the lobar bronchus.

The location of the tumor and its rate and extent of spread are apparently related to the cell type. The cell type is an important factor in the ultimate prognosis, although prognosis cannot be determined from this factor alone in any given patient.

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Pseudocyst Formation in Chronic Pancreatitis

A Cause of Obstructive Jaundice

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Obstructive jaundice in the adult is usually caused by biliary tract calculi or neoplasms, hepatotoxic drugs, and, less commonly, a cholangiolitic form of infectious hepatitis. An uncommon cause is biliary obstruction from a pancreatic pseudocyst. The importance of considering compression of the common bile duct by a cyst in the head of the pancreas is the problem of differentiating this lesion from carcinoma. This separation, often impossible by clinical and laboratory methods, is frequently difficult at the time of laparotomy. The diagnostic and therapeutic aspects of this cause of jaundice are illustrated by the present report.

Report of a Case

A 52-year-old white, married, male hospital housekeeper, was admitted to the Peter Bent Brigham Hospital for the first time in July, 1957, because of jaundice of three days' duration. A chronic alcoholic, he had been in good health until eight months before admission. Since that time he had noted intermittent epigastric and right upper quadrant pain, which radiated to the back and was aggravated by food or alcohol. Four months before admission diabetes mellitus was demonstrated. A cholecystogram and upper gastrointestinal x-ray study were normal. Stools had been light, bulky, and malodorous, and he had lost 40 lb. in weight. Severe pruritus began three weeks before admission. Jaundice was first discovered by his wife three days before entry. He denied the ingestion of hepatotoxic drugs, injections, and exposure to jaundiced persons. There was a family history of diabetes mellitus.

On admission the vital signs were normal. He appeared chronically ill and was icteric. There were no stigmata of liver disease. The abdomen was relaxed and soft, with a smooth, nontender liver, palpable 2 fingerbreadths below the right costal margin. There was no palpable mass or tenderness, and the spleen was not palpable. The remainder of the examination was normal.

He had a negative serologic test for syphilis, a hematocrit of 44%, a sedimentation rate of 40 mm. in one hour (Wintrobe), and a leukocyte count of 7000 per cubic millimeter, with a normal differential. The urine was normal except for the presence of bile and glucose. Serum bilirubin was 8.6 mg. % (6.0 mg. was direct, 2.6 mg. was indirect), alkaline phosphatase 16 Bodansky units, thymol turbidity 26 units (normal), calcium 5.1 mEq/L., phosphorus 1.2 mM/L., amylase 24 units (normal), and fasting blood sugar 280 mg. %. The serum albumin was 3.5 gm. % and globulin 3.1 gm. %; cholesterol, 185 mg. % with 56% esters, and the prothrombin activity was normal. The stool was yellow and contained undigested muscle fibers and showed a 3+ reaction to benzidine. Fecal fat was 21, 14, and 31 gm. per day on a diet containing 70 gm. of fat; normal is less than 4 gm. a day. Absorption of butter fat was markedly decreased. Xylose absorption was normal. Examination of duodenal fluid did not demonstrate lipase, amylase, trypsin, tumor cells, or cholesterol crystals. X-ray studies showed diffuse pancreatic calcification and widening of the duodenal loop.

The hospital course was characterized by clearing of the jaundice. Twelve days after the admission his abdominal pain had decreased, his appetite was good, and there was still no abdominal mass palpable. The bilirubin had fallen from 8.6 to 2.4 mg. %, and the alkaline phosphatase, from 15.6 to 9.2 Bodansky units. His diabetes was difficult to control. He required up to 70 units of isophane (NPH) insulin plus 35 units of zinc insulin crystals (N. N. D.) daily. It was felt that the clinical features were consistent with

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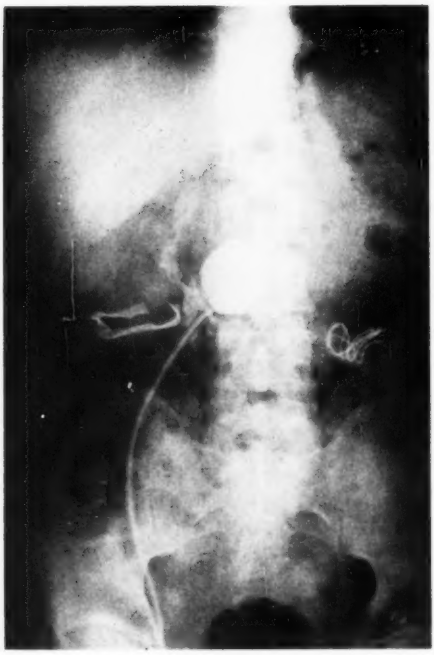

Fig. 1.—Pancreatogram made at the time of laparotomy. A large unilocular cyst in the head of the pancreas is seen.

chronic pancreatitis with pancreatic insufficiency. A laparotomy was performed to exclude a neoplasm or biliary calculus.

Operative Findings.—Exploration of the abdomen showed a mass in the head of the pancreas. The mass was firm, measured 5 cm. in diameter, and appeared slightly cystic to palpation. The common duct was dilated, with a diameter of about 1.5 cm. The gallbladder was distended, and compression produced no emptying. There were no palpably enlarged lymph nodes, and the liver and stomach were normal. On the medial wall of the duodenum an ulcer crater was palpable.

The common duct was opened and no stones were demonstrated, but a probe could not be passed into the duodenum. The head of the pancreas and the duodenum were mobilized, and the second portion of the doudenum was opened. The ulcer on the medial wall lay against the pancreatic mass and was shallow, soft, and appeared to have granulation tissue in its base. A biopsy specimen of this was taken, after which a probe was passed through the base of the ulcer, and apparently into the mass, because there was a sudden flow of 60 to 70 cc. of clear fluid. The mass suddenly collapsed, and the common-duct probe readily passed into the duodenum about 1 cm. above the ulcer. A fine catheter was inserted into the mass, and a pancreatogram was made, which demonstrated a large unilocular cyst (Fig. 1). The catheter tract was explored with the finger, and a pseudocyst of the head of the pancreas, with inflammatory tissue as its lining, was encountered. Adequate internal drainage was achieved by this maneuver, which produced a cystoduodenostomy. The sphincter of Oddi was incised because a "common channel" for the main pancreatic duct and the common bile duct was observed. Definitive drainage of the common duct was accomplished by a choledochojejunostomy, using a Roux-Y loop of jejunum placed side-to-side with the common duct. Biopsy specimens of the pancreas were taken by needle and direct-wedge technique. Following placement of the cholecystostomy tube and a catheter in the common duct through the choledochojejunostomy opening, the abdomen was closed.

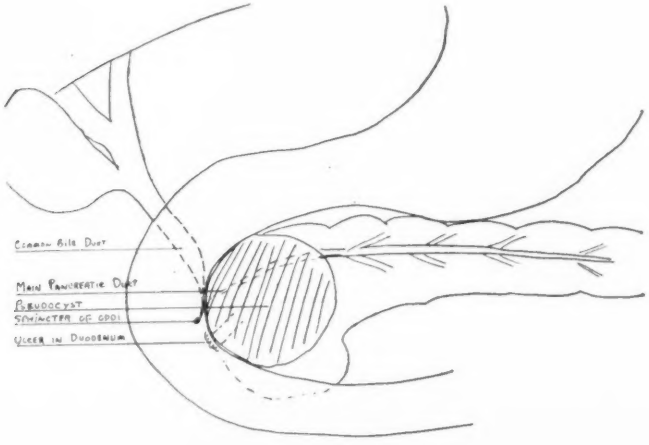

Fig. 2.—Diagram of the relationship of the pancreatic pseudocyst to the common bile duct and the main pancreatic duct.

TABLE 1.—*Causes of Jaundice in Chronic Pancreatitis*

I. Jaundice associated with pancreatitis
  A. Hepatocellular disease*
  B. Biliary tract disease
    1. Calculi
    2. Cholangitis
  C. Compression of the intrapancreatic common bile duct
    1. Edema or inflammation
    2. Fibrosis or calcareous changes
    3. Cyst or Pseudocyst of the pancreas
II. Jaundice unrelated to pancreatitis
  Carcinoma, hepatotoxic drugs, hepatitis, surgical trauma to the biliary tract

Pathologic Findings.—The pancreatic tissue showed chronic inflammation, fibrosis, ductal dilatation and lithiasis, and squamous metaplasia of the ductal epithelium. None of the four biopsy specimens of the pancreas showed any evidence of malignancy. A lymph node from the transverse mesocolon was normal. The floor of the ulcer at the base of the ampulla of Vater showed acute papillitis.

The pathologic process may be summarized as chronic pancreatitis with a pseudocyst of the head of the pancreas, which was responsible for obstruction of the common bile duct and pancreatic duct on a mechanical basis, as shown in Figure 2. It appears that the cyst was eroding into the duodenum by pressure necrosis. Spontaneous drainage might occur by such a mechanism.

Postoperative Course.—The icterus cleared, and the patient's insulin requirement fell rapidly to 30 units of isophane insulin. A cholangiogram on the 12th day following surgery demonstrated a normal common bile duct, and there was rapid filling of the duodenum and the jejunum. At this time the cholecystostomy tube was removed. The common duct tube was removed two days later. His stools were brown and no longer foul or bulky. He was discharged on the 19th day after surgery. He returned to work and gained 14 lb. during the next two months. He has been free of abdominal pain, tenderness, and jaundice.

Comment

The problem presented is that of obstructive jaundice in an alcoholic with known chronic pancreatitis. Jaundice is not uncommon in chronic pancreatitis. Cattell and Warren [1] noted jaundice in 26% of the cases observed at the Lahey Clinic. Haggard and Kirtley [2] reported jaundice in 18 (28%) of their 65 collected cases. The causes of jaundice in a patient with chronic pancreatitis are summarized in Table 1. In a review of 1035 patients with jaundice associated with pancreatic disease, Fraser [4] found that in 1.2% the cause was a pancreatic cyst.

The exact incidence of pseudocyst formation in chronic pancreatitis is unknown. Shingleton [5] states that 5%-10% of these patients develop a pseudocyst which requires treatment. Physical or x-ray evidence of a mass in the region of the pancreas in a patient with pancreatitis suggests a pseudocyst. The absence of these findings does not exclude it.

Jaundice associated with pseudocysts was found by Judd [6] in 21% of 47 cases, by Adams and Nishijima [7] in 33% of 9 cases, by Brilhart and Priestley [8] in 30% of 44 cases, and by Cattell and Warren [9] in 13% of 46 cases. In an earlier review of 304 patients with cysts of the pancreas, Brunschwig [10] noted that jaundice was described in 5%-10%. This indicates that jaundice may be encountered in 5%-30% of patients with pancreatic pseudocysts.

Rarely can the jaundice be related causally to ductal compression by the pseudocyst. To establish this direct relationship the following criteria are required: (*a*) presence of obstructive jaundice; (*b*) operative demonstration of compression of the common bile duct by a cyst; (*c*) relief of bile duct obstruction by surgical drainage of the cyst, and (*d*) complete clearing of the jaundice. The case described above fulfills these criteria. Other cases in the literature which fall into this pattern are summarized in Table 2.

In addition to the present report, Cases 1 and 2 of Table 2 and 9 of the 121 collected cases of pseudocyst described by Korte (cited by Cattell and Warren [9]) were the only ones found which appear to fulfill the criteria for a cause-and-effect relationship. The other cases are included as examples of icterus associated with pseudocyst in which compression of the common duct was the probable cause. Several important points are illustrated. Case 1 indicates that pseudocyst formation may exist without pancre-

TABLE 2.—*Cases of Jaundice Associated with Pseudocyst in the Head of the Pancreas*

Case No.	Author	Age	Sex	Duration of Icterus	Cyst in Head of Pancreas	Surgical Procedure	Postoperative Result
1	Carter and Slattery[1]	40	M	2 mo.	Compressing common bile duct	Excision	Symptoms relieved
2	Cattell and Warren[3] (Case 9)	51	M	3 wk.	Medial to common duct	Pancreatoduodenectomy	Symptoms relieved
3	Pinkham[13] (Case 2)	57	M	1 yr.	Large; 2000 cc.	Marsupialization	Discharged well
4	Pinkham[13] (Case 3)	45	F	2 yr.	In lesser sac	Simple drainage	Discharged well
5	Adams and Nishijima[1] (Case 5)	45	M	3 days	6 cm. in diam. in curve of duodenum	Cystojejunostomy	Symptoms relieved
6	Johnson and Lee[14] (Case 5)	68	F	5 wk.	3 cm. in diameter	"Drainage"	Discharged well
7	Doubilet and Mulholland[15] (Case 3)	40	M	Present	Large	Cystojejunostomy	Discharged well
8	Chesterman[16]	39	F	1 wk.	In lesser sac	Cystojejunostomy	Symptoms relieved
9	Hardy and Bowlin[17] (Case 6)	50	M	1 mo.	10×10 cm. mass	Lymph node biopsy	Spontaneous improvement
10	Present case	52	M	3 days	5×5 cm.	Cystoduodenostomy	Symptoms relieved

atitis. In Case 2 a pancreatoduodenectomy was performed because the pseudocyst was interpreted in the gross specimen as carcinoma of the head of the pancreas. In Case 9 the probable pseudocyst was interpreted as carcinoma of the head of the pancreas on the basis of a frozen section of an adjacent lymph node, and no corrective procedure was performed. Brilhart and Priestley[5] state that in only 9 of their 44 cases was the diagnosis of pseudocyst of the pancreas made preoperatively. In two of these a "Whipple-type" procedure was done. The authors state: "This procedure is not recommended for pseudocyst of the pancreas which is recognized as such at the time of operation." Fraser[4] reports that in his series of 1035 cases of obstructive jaundice due to pancreatic disease, 7% were "benign lesions" mistaken for malignant disease. Contrariwise, 16% of malignancies were interpreted as benign lesions at the time of surgery.

The presence of diabetes mellitus is not of help in differentiating pancreatic cyst and carcinoma. Cliffton,[18] in a review of 78,249 cases of pancreatic carcinoma, noted diabetes in 25%. Cattell and Warren[3,9] state that diabetes may be present in 33% of patients with relapsing pancreatitis and in 10%-20% of patients with pancreatic cysts.

Preoperatively, in the present case, it was known that pancreatitis was present. The nature of the mass demonstrated by x-ray in the region of the duodenal loop was unknown. Furthermore, at the time of surgery the gross features suggested carcinoma. Because the mass had a slightly cystic nature, a duodenotomy was performed. This was associated with rupture of the cyst, revealing the true nature of the lesion.

Fallis and Szilagyi[19] state:

> The absence of marked reduction of pancreatic enzymes in duodenal drainage as described by Whipple and his associates in conjunction with evidence of obstructive jaundice is strongly suggestive of carcinoma of the head of the pancreas.

The present report indicates that this same phenomenon may occur with a pancreatic cyst which occludes the pancreatic duct.

The cases summarized illustrate the effectiveness of surgical procedures in correcting the bile duct obstruction caused by a pseudocyst. These surgical approaches include the classical excision and marsupialization procedures and the more recent methods for internal drainage, typified by the cystoduodenostomy used in the present case.

Summary

A case of obstructive jaundice complicating chronic pancreatitis, with pancreatic insufficiency and diabetes, is reported. The jaundice was caused by common bile duct obstruction from a pseudocyst in the head of the pancreas, which was demonstrated at laparotomy. Cystoduodenostomy and choledochojejunostomy provided drainage of the cyst and clearing of the jaundice.

This cause of obstructive jaundice should be suspected in patients with chronic pancreatitis and in patients with a mass in the region of the head of the pancreas. The recognition of pancreatic pseudocysts is important because of the difficulty in differentiating this lesion from carcinoma of the pancreas, and because correction is possible by specific surgical procedures.

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Diffusion of Oxygen and Carbon Dioxide Through Teflon Membranes

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It has been shown by Clowes that the construction of a membrane oxygenator is practicable and that thin Teflon membranes permit greater passage of oxygen than any others now available.[1] Clinical studies with the membrane oxygenator have utilized a polyethylene membrane 0.0008 in. thick. In such an oxygenator the passage of both oxygen and carbon dioxide apparently were satisfactory. According to Clowes, carbon dioxide was found to diffuse from blood through Teflon at rates proportional to oxygen uptake. Limited studies in the laboratory with a small modified Clowes oxygenator led us to the belief that carbon dioxide, at reasonable pressures, diffuses to an inadequate degree through Teflon membranes. This belief appears to be substantiated by the following studies.

Materials and Methods

Oxygen transfer through Teflon membranes 0.00025 to 0.004 in. thick was studied by means of a platinum polarograph. The Clark electrode[2] was used, and the amplified electrode current was recorded directly.* The oxygen electrolyzed at the platinum cathode was then calculated, and the results were converted to oxygen transfer in cubic centimeters per minute per square meter of membrane as follows:

$$O_2 \text{ electrolyzed, in gm/sec.} = \frac{iW}{nF}$$

where i=electrode current, in amperes

F=the faraday (96,000 coulombs or ampere-seconds), the current required to reduce 1 gram-equivalent

W=the molecular weight of oxygen (32)

n=the number of electrons required to reduce one molecule of oxygen. This is probably 4, the reaction being as follows:[3]

$$2H^+ + O_2 + 2e \longrightarrow H_2O_2$$
$$2H^+ + H_2O_2 + 2e \longrightarrow 2H_2O$$

$$O_2 \text{ in cc/sq. m/min.} = \frac{iW}{nF} \times \frac{10^3}{D} \times \frac{10^6}{a} \times 60$$

where D=density of oxygen in gm/liter=1.25 at 37° C

a=area of Clark electrode, in square millimeters. Since platinum face is 2 mm. in diameter, area is 3.14 sq. mm.

The effect of temperature on the transfer of oxygen was studied between 20 and 40° C. using warm air.

During various laboratory procedures, including some total and some partial cardiopulmonary bypasses, venous blood going to and arterial blood leaving the oxygenator were sampled and analyzed for carbon dioxide and oxygen by the Van Slyke method. These data were used to gain information concerning the actual transfer of these gases under relatively physiological conditions. The details of the circuits, etc., are reported elsewhere.[4,5]

Additional information regarding carbon dioxide transfer was obtained with a closed circuit consisting of a small bubble oxygenator, a Sigmamotor pump and a 0.5 sq. m. area membrane oxygenator. An excess of 5% carbon dioxide in oxygen was delivered to the small bubble oxygenator† to supply a stable partial pressure of carbon dioxide in water. The Sigmamotor pump was set occlusively for 200 cc. per minute. Five liters of oxygen per minute was supplied to the membrane oxygenator. Samples for analysis by the Van Slyke method were drawn at approximately 15-minute intervals from the inlet and the outlet of the membrane oxygenator.

Most of the tests were done on Teflon membranes, but a few studies on unknown commercial samples of polyethylene and cellophane were carried out also.

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From the Research Laboratory of the East Tennessee Tuberculosis Hospital and the Department of Surgery of Acuff Clinic.

* Apparatus which is used with the Sanborn recording equipment was constructed by George Peirce, University of Pennsylvania School of Medicine; electrodes made by Yellow Springs Instrument Company, Antioch, Ohio.

† Selas Corp., Dresher, Pa.

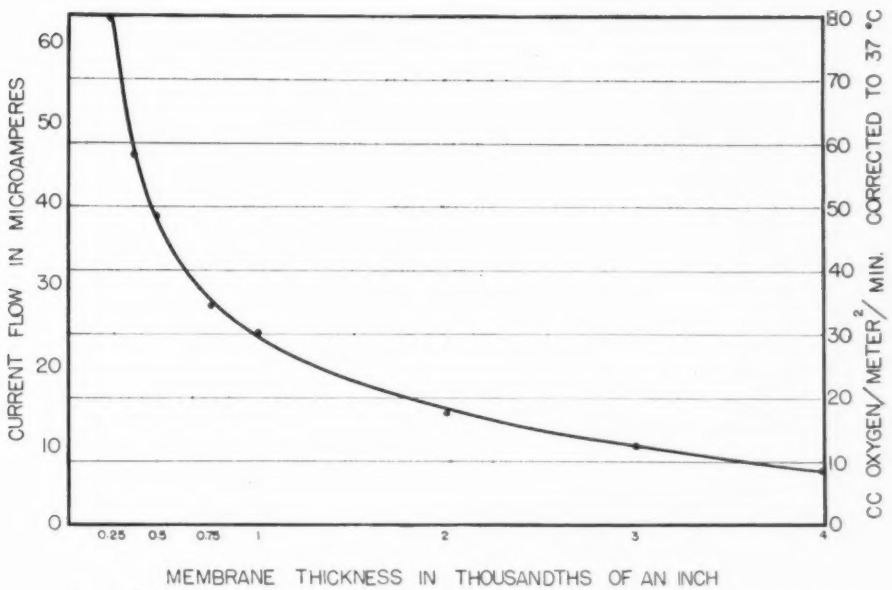

Fig. 1.—Diffusion of O_2 through Teflon membranes as measured by current flow in a platinum electrode (Clark). Temperature 20 C.

Results and Comment

The values for oxygen diffusion obtained with the polarograph are shown in Figure 1. The data were corrected to 37 C and a pO_2 of 760 mm. Hg. These figures are approximately twice those reported by Clowes. Using a diffusion chamber, he measured the most rapid rates of diffusion of oxygen into agitated blood at 33-34 C. For 0.0005 in. Teflon a maximal value of 25.5 cc. of oxygen per square meter per minute was found. In actual use in a small oxygenator this figure was reduced to 21.8 cc., using a blood flow of 200 cc. per square meter.

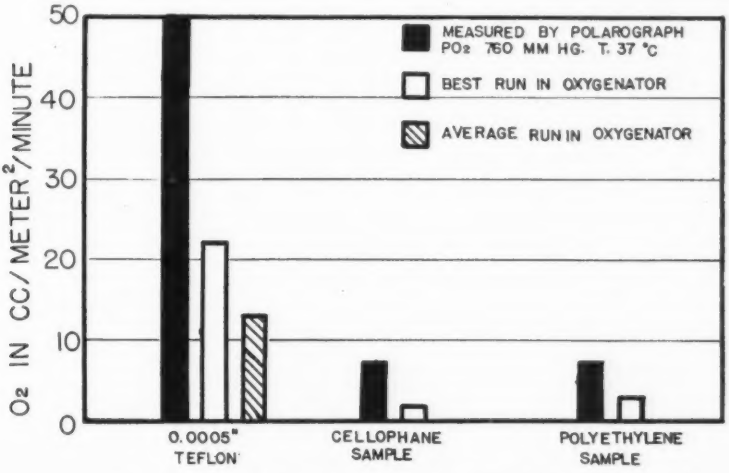

Fig. 2.—Oxygen transmission through various membranes.

These data also approximate our own for blood (Fig. 2). Three main factors are believed to contribute to the discrepancy between the polarographic and the oxygenator data.

1. The blood channels in the Clowes oxygenator are relatively large, leading to some streamlining, and possibly some venous shunting. This would be expected to produce a marked reduction in the effective gradient between oxygen and blood. Narrower, shorter blood passages would improve the efficiency of the oxygenator, though pressure and flow problems would be created.

2. It is not possible using blood to maintain an oxygen gradient across the membrane equal to the gradient with the Clark electrode in 100% oxygen. The pO_2 at the electrode interface is zero,[3] whereas the pO_2 of blood varies from 20 to 100 mm. Hg or more. An average correction would be 7% to 15% of the polarographic reading.

3. The values obtained with the polarograph are subject to several minor errors. The effective area of the Clark electrode is probably a little larger than that calculated from the diameter of the platinum, owing to the presence of an incompletely covered edge. In addition, the reading of the electrode current is subject to some error. These factors together should not exceed 10%.

Results obtained with unknown, commercially obtained samples of cellophane and polyethylene are compared with Teflon in Figure 2. The polyethylene used extensively by Clowes measured 0.0008 in. in thickness and in the oxygenator transmitted roughly one-third as much oxygen as 0.0005 in. Teflon. Presumably, this polyethylene was about half the thickness of the sample tested by us. An interesting feature of the cellophane was that oxygen transmission was very poor until the membrane had been wet by placing it in saline, although it appeared to be a relatively nonwettable variety. Following this, the polarographic reading in air approximated that of the polyethylene.

Figure 3 gives the data on transfer of carbon dioxide through 0.0005 in. Teflon and through our samples of cellophane and polyethylene. Five Van Slyke measurements are combined for the Teflon reading. Single measurements were made for the other two membranes. The partial pressure of carbon dioxide was corrected for the barometric pressure and the partial pres-

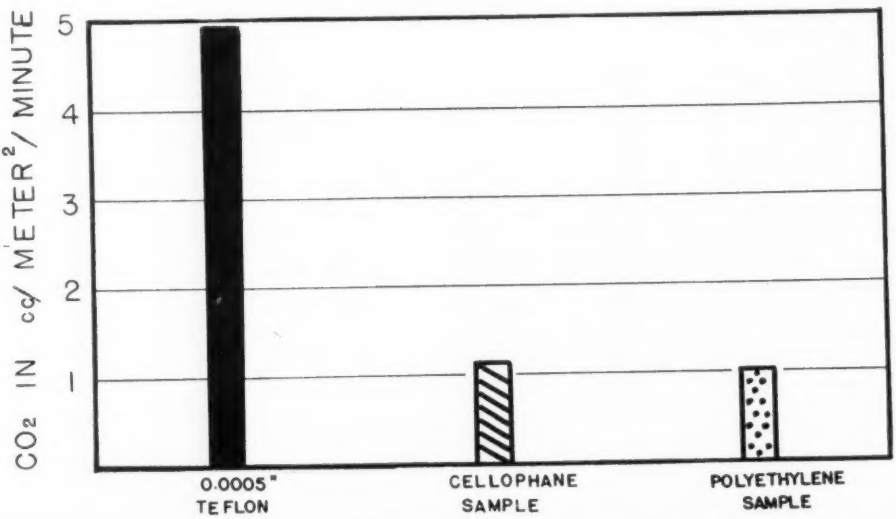

Fig. 3.—Carbon dioxide transfer through various membranes; pCO_2 36; temperature 37 C.

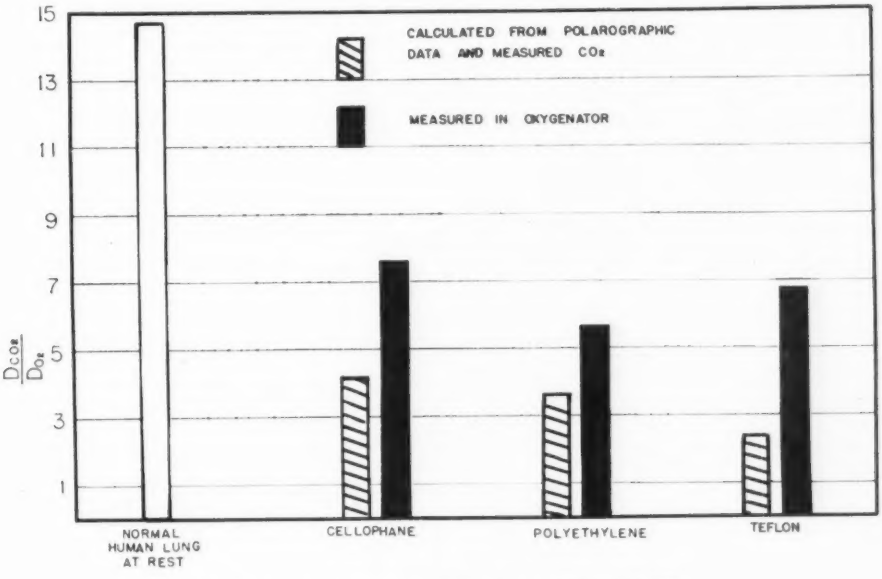

Fig. 4.—Diffusion coefficients of CO_2 and O_2 compared for various types of membranes.

sure of water vapor at the temperature of the experiment. It can readily be seen that the transmission of carbon dioxide was markedly less than that of oxygen.

The diffusion coefficients of carbon dioxide and oxygen are compared in Figure 4. The amount of carbon dioxide transferred through Teflon, polyethylene, and cellophane per millimeter Hg pressure per minute is greater than the amount of oxygen transmitted per millimeter per minute. In the Clowes oxygenator, however, the partial pressure of oxygen is approximately 15 to 20 times that of carbon dioxide. This results in a deficiency in the transfer of carbon dioxide for all of the membranes studied.‡

The ratio of the diffusion coefficients is given for the human lung also, for comparison. It would appear that even for this remarkably efficient organ raising the oxygen tension to 760 mm. of Hg would result in a relatively less efficient transmission of carbon dioxide than of oxygen.

The explanation for the above figures can be found by studying the behavior of carbon dioxide and oxygen in solution and comparing it with their behavior as dry gases.

The rate of diffusion of a gas through a liquid is directly proportional to the absorption coefficient (solubility) of the gas in that liquid and is inversely proportional to the square root of its molecular weight. The coefficient of absorption of oxygen in plasma at body temperature is 0.024 and of carbon dioxide 0.510. The diffusion rate of carbon dioxide through a wet membrane is, therefore, about 30 times as great as that of oxygen when the gases are under identical conditions. The rate of the diffusion of a gas into another gas varies with the partial pressure and is inversely proportional to the square root of its molecular weight. In dry air, carbon dioxide, therefore, diffuses less rapidly than oxygen, the factor being about 0.85. It should be expected, then, that the

‡ Wettable cellophane (DuPont PD 300) has a diffusion coefficient for CO_2 23 times as great as that for O_2 and therefore would be expected to show adequate CO_2 transfer in the Clowes oxygenator.[8]

wettability of a membrane would greatly affect the way in which carbon dioxide and oxygen diffuse through it. The ratio of the diffusion coefficients should show the qualitative differences in membranes best, since the absolute amounts of gas, which depend on molecular configuration, membrane thickness, etc., would not be involved. Various membranes are compared in Figure 4. It is noteworthy that the normal human lung approaches the value expected for a wet membrane, while Teflon, a membrane which does not absorb appreciable water, approaches the theoretical value for a dry membrane. The data which, of course, are inadequate for cellophane and polyethylene, suggest that these membranes are, in fact, somewhat wettable.§

Our findings call to mind another oxygenator which has somewhat the same problem as a membrane apparatus. The small-bubble oxygenator, developed by Gollan, Clark, and Gupta,[8] is an extremely efficient oxygenator but, because of the relatively small tidal volume of gas required, eliminates carbon dioxide very poorly. It has been found necessary to supplement the gas flow, which may be done with much larger bubbles, to provide for the elimination of carbon dioxide. The net result of this supplementation is, of course, to reduce the remarkable efficiency of oxygenation of this apparatus. Similarly, it appears likely that, in order to provide adequate carbon dioxide exchange in the membrane oxygenator, it will be necessary either to find a strong, wettable membrane of good oxygen transmission or to reduce the effective diffusion of oxygen to the point where it does not greatly exceed the carbon dioxide elimination. An analogy can be found in the hypercapnia produced during anesthesia because of inadequate respiratory exchange. In such instances, when the patient is supplied with 100% oxygen, he may be fully oxygenated, while carbon dioxide retention reaches dangerous levels. For the present, therefore, it will be safer to keep the oxygenator relatively inefficient as far as oxygenation is concerned so that carbon dioxide diffusion will be sufficient.

According to Clowes, "carbon dioxide tension rises unless the blood is being delivered at a level of more than 85% oxygen saturation."[9] This would appear to confirm the low carbon dioxide transfer and the need for keeping oxygenation inefficient. Where oxygen diffusion is greatest, over the straight portion of the hemoglobin-dissociation curve, carbon dioxide diffusion lags. It is only when oxygenation is carried out in the upper part of the curve, where large pO_2 changes are necessary for small transfers of oxygen, that carbon dioxide can catch up. In addition, the tendency for pH to drop some with the membrane oxygenator because of CO_2 retention results in a decreased efficiency of oxygen transfer and an increase in carbon dioxide diffusion, bringing about a more favorable balance between oxygenation and carbon dioxide elimination.

The elimination of carbon dioxide might be expected to be even less satisfactory under conditions of hypothermia when a membrane oxygenator is employed. This is true for an oxygenator using polyethylene or cellophane, since gas diffusion falls sharply with reduced temperatures. Using a Teflon membrane, however, there is very little decrease in diffusion at lower temperatures. In addition, as the temperature falls, the solubility of carbon dioxide rises sharply, the pCO_2 declines, and carbon dioxide retention is better tolerated. A final favorable factor in hypothermia is a pH rise of 0.0147 unit for each degree (centigrade) of fall. This permits adequate oxygenation at lower oxygen pressure.[10]

Summary

The platinum polarograph provides an accurate method of measuring oxygen transmission through different membranes.

§ There is considerable evidence that the above explanation is an oversimplification. It is quite possible that wetting a membrane leads to molecular rearrangement of the plastic and that it is this, and not the presence of water, which changes the diffusion of the gas.[7]

High oxygen transmission through Teflon membranes is confirmed.

Measured values of oxygen transmission for a Clowes-type oxygenator are approximately one-third to one-half those obtained by polarographic measurements. This discrepancy is discussed.

The measured transmission of carbon dioxide through Teflon is very low compared with the figures obtained for oxygen at physiological pressures. Behavior of the two gases is dissociated and depends on their individual partial pressures. Data are presented which suggest that diffusion of gases through Teflon membranes can be predicted best from the behavior of the gases in dry air. This is important, since diffusion through biological membranes depends on the behavior of gases in liquids. Apparently, use of the dry membrane Teflon in an oxygenator results in carbon dioxide retention. The data indicate that the samples of cellophane and polyethylene tested are only slightly wettable, and also show relatively poor ability to transmit carbon dioxide. Wettable cellophane has a favorable diffusion ratio.

It is suggested that no present benefit can be derived from improved oxygenation in membrane oxygenators because the limiting factor is the diffusion of carbon dioxide. A Teflon oxygenator, for instance, must be used at less than 25% efficiency as far as oxygenation is concerned to prevent carbon dioxide retention.

Because of the decrease in metabolism and the increase in solubility of carbon dioxide in hypothermia, the membrane oxygenator should prove to be a satisfactory apparatus to use in conjunction with cooling. This is particularly true for Teflon, which shows little decrease in gas diffusion as the temperature falls.

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Recipient Set for Removal of Potassium and Ammonium from Bank Blood

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This paper describes a simple device for removing excess potassium and ammonium ions from bank blood during transfusion.

A progressive rise in the concentration of potassium and ammonium occurs in whole blood during storage.[1-3] This takes place regardless of the original method of collection.[3] During most transfusions, excessive potassium and ammonium in bank blood are diluted by the patient's blood, and thus are well tolerated. However, when large volumes of blood are needed rapidly to combat oligemia, the effect from elevated levels of these electrolytes becomes increasingly hazardous.

Keith and Osterberg[4] reported marked intolerance to exogenous potassium in patients with advanced renal insufficiency. During the Korean War, studies on renal failure following severe wounding revealed that the hyperkalemia resulting from extensive tissue destruction was greatly aggravated because of multiple transfusions with old bank blood.[5] Some cardiac arrhythmias during massive blood replacement may be on the basis of hyperkalemia,[6] and Watkins[7] suggested that this increased sensitivity of the heart might be due to an elevation of extracellular potassium in the myocardium during hypotension.

Cincotti[8] attributed the hepatic coma which ensued in patients with portal cirrhosis receiving liberal amounts of blood to excessive ammonium in the transfused blood. We observed an increase of more than 100% in the circulating ammonium level of two patients with portacaval shunts, each of whom received 6 pt. (3 liters) of 21-day-old blood. The blood ammonium returned to a normal range in both instances after the transfusions were discontinued. One of these patients had a blood ammonium level of 114μg. % before transfusion. After receiving blood containing 1179μg. % of ammonium his blood level increased to 413μg. %. Two hours after the administration of blood was discontinued, the level was 229μg. %, and after four hours, 142μg. %.

Both potassium and ammonium can be extracted from bank blood by passage of the latter through a column of a cation-exchange resin.[9] More than 90% of potassium and 70% of ammonium can be removed by a single passage across the resin. Calcium and magnesium are also removed, but to a less extent, and these substances may be readily replaced. The ion-exchange packs available commercially at present are equipped with plastic containers as single units. The incorporation of such a unit in series with the container of bank blood involves using an additional blood administration set and container. In an attempt to reduce the expense and bulk of such a system, we have designed the recipient set illustrated in the Figure. This device* removes excess potassium and ammonium from bank blood while it is administered to a patient.

The coupler fits into either standard bottle or plastic containers. It has a 4 mm. diameter and is 3 cm. long, this shortness and

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Post Doctorate Research Fellow, National Institutes of Health (Dr. Schechter).

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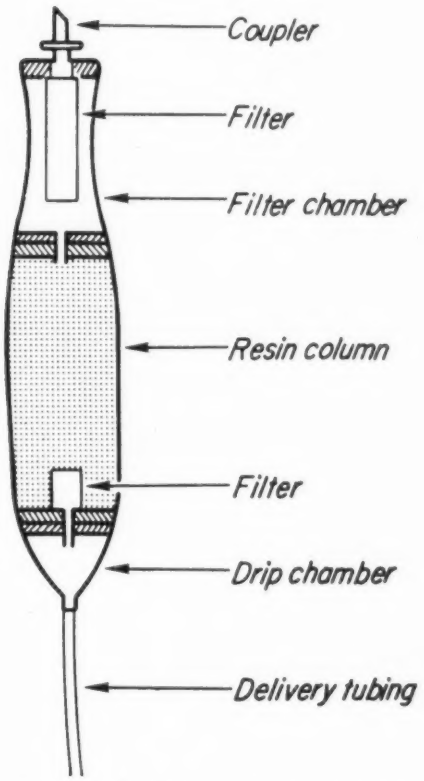
* Fenwal Laboratories, Somerville, N. J.



The modified recipient set incorporates a column of cation-exchange resin which removes accumulated potassium and ammonium from bank blood during its administration.

wide lumen permitting the easy passage of any fibrin present in the blood.[1] The filter chamber is 8 cm. long, 2 cm. in diameter, and has a wall 0.5 mm. thick. The filter consists of 70×70 mesh nylon and has an area of 32 sq. cm. The filtered blood crosses the ion-exchange resin, which is in a column in tandem with the filter chamber. This column, which consists of a casing of the hemorepellent plastic Vinylite, is approximately 12 cm. long, 3.5 cm. wide, and 2.8 cm. in diameter, has a 0.5 mm. wall, and contains 50 gm. of Dowex-50-×8 (a cation exchange resin), sodium cycle. The resin is supported on 100-mesh nylon bolting cloth to prevent entrainment distally of the resin spherules, which are of 50-mesh dimension. Below the resin column is a 5 cm. long-drip chamber with a 0.5 mm. compressible wall.

We have tested this apparatus on nine containers of blood collected in anticoagulant acid citrate dextrose (A. C. D.) solution U. S. P., Formula B (Transfuso Vac, Baxter Laboratories), and on nine others collected in anticoagulant acid citrate dextrose solution Formula A (ACD Blood Pack, Fenwal Laboratories). Our laboratory device differed from the one described above only in that the drip chamber (a nonfunctional component of the system) was proximal to the resin column. Satisfactory potassium and ammonium extractions were obtained at different flow rates. Optimal performance appears to occur if the blood does not cross the resin at rates exceeding 50 ml. per minute. This rate, of course, is much greater than the rates ordinarily employed in most transfusions, so that enhanced efficiency of extraction may be expected with routinely used flow rates. If, however, intra-arterial infusions are necessary, the "deionized" blood may be collected prior to transfusion in a plastic container (Transfer Packs, Fenwal Laboratories), and rapid administration under pressure is then effected by manual or other mechanical compression of the plastic pack.

Summary

A recipient set for use during blood transfusion is described which combines the features of both a filter-and-drip chamber and a cation-exchange resin column. This single-unit device can be used to remove excess potassium and ammonium from stored blood while it is being administered.

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Freeze-Dried Arterial Homografts

Details of Technique of Processing and Analysis of Vessels Used Over a Two-Year Period

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Introduction

The concept of an artery bank for processing, storing, and distributing homologous arteries has become well established in recent years. Units to prepare vessels for use as homografts have appeared in many parts of the country, and some of the progress that has been made in the field of vascular surgery in the last few years can be attributed to the existence of these banks, which have made available to surgeons a supply of homografts.

That arterial homografts have been and continue to be of great importance in vascular surgery no one will deny. Their future is still obscure, however, in that much progress has been made in the use of synthetic materials as vessel prostheses and developments along these lines are sure to continue. The ready availability of a manufactured product is a great inducement to use of the synthetic grafts, but it would be wrong to base the decision as to the type of graft that will be used in the future simply on this one aspect. Just what type of graft will ultimately be generally accepted as the best is still hard to say, and a number of years may still be required before long-term studies give us information regarding the function of the various types of vessel grafts. Certainly, until a synthetic material has been developed which proves highly satisfactory both in the operating room and over an adequate follow-up period, the facilities for obtaining, processing, and storing homografts should be maintained and perfected.

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The purpose of this paper is not to discuss the relative merits of homografts and synthetic grafts, or the many approaches to the technical problem of preserving arterial segments for later use. Rather, it is to present the procedure which has been used over the last two years at the Northern California Artery Bank, together with a follow-up on the vessel segments used thus far by the surgeons in the area making use of the Bank.

Processing Method

The basic physics behind the methods used have been applied specifically to this field by Sauvage,[1] Hufnagel,[2] and others. The apparatus which was designed for this bank was based on the theoretical consideration and practical applications as defined by these workers, and adaptations and developments have been worked out so as to devise a satisfactory technique which can be learned and carried out by a technician with the minimum of hazards and with the assurance that the vessels being processed will be satisfactorily prepared. The method of processing will be presented for those about to set up an artery bank, or to modify one that already exists. Essentially, the procedure utilizes ethylene oxide gas to sterilize the segments, which are then frozen, dried, and stored in nitrogen gas at room temperature.

In preparing the vessel segments for processing, care should be taken to leave the branches from the main artery at least 5 mm. long, so that they can be easily ligated at a later date in the operating room. Also, a careful inspection of the vessel segments

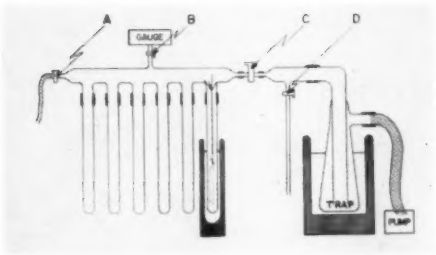


Fig. 1.—Freeze-drying apparatus diagrammed, with the stopcocks *A*, *B*, *C*, and *D* mentioned in the text.

may reveal traumatic or arteriosclerotic defects, thus rendering that segment unfit for use. If histological examination is to be carried out on the vessel, a small segment is removed at this time.

Each vessel is then suspended in the manifold in its individual tube by means of a thread, together with a small piece of tissue to be tested later for sterility. The tubes are sealed to the manifold by the steel-ring vacuum couplings.

After the vessel segments have been suspended in the lower half of the tubes, and with stopcocks, *A*, *B*, and *D* closed and *C* open, a very slight vacuum is built up in the manifold by means of the pump. After about a minute the pump is stopped; stopcock *C* is closed, and the glass ampule containing ethylene oxide is taken from the refrigerator and attached to the polyethylene tube connected to stockcock *A*. Stopcock *A* is then opened, and the ethylene oxide, when warmed to about room temperature, boils slowly, and the gas passes into the manifold. Within a very few minutes the vessels take on a shiny, oily quality, indicating that they have become completely coated by a layer of ethylene oxide. When this has taken place, stockcock *A* is closed and the ethylene oxide ampule is capped and returned to the refrigerator. Altogether, only about 5 to 10 cc. of the liquid is required for each procedure. The gas is left exposed to the vessels for a period of 30 to 40 minutes, and then the tube attached to stopcock *A* is connected to one which leads out a window. After stopcocks *C* and *D* have been opened, the ethylene oxide gas is blown out of the manifold and out of the window by means of compressed nitrogen gas fed in through stopcock *D*. Stopcock *B* is closed during this stage to keep the gas out of the vacuum-gauge apparatus; it is open for all subsequent stages.

This method has the advantage that the toxic and explosive gas is thus always in a closed system and the technician is never in contact with the liquid or the gas. We have never had any difficulties in using this method; and, although cultures are run on every segment processed, we have obtained positive cultures on only 6 out of 425 processed segments, and we have heard of no graft difficulties that could in any way be attributed to nonsterile grafts.

When the ethylene oxide has been blown out of the system, stopcocks *A* and *D* are closed, *C* is left open, and *B* is opened. Using an ethylene glycol-carbon dioxide snow (dry ice) mixture in an individual long, narrow Dewar flask, the vessels are quick-frozen by lifting the flasks up around the tubes, so that all the vessel in the tube is below the freezing mixture. The Dewar flask is supported in position by a ring-stand form of holder. When all vessels have been frozen, liquid nitrogen is placed in the large Dewar flask surrounding the vapor trap, the pump is started, and the vacuum is built up in the system.

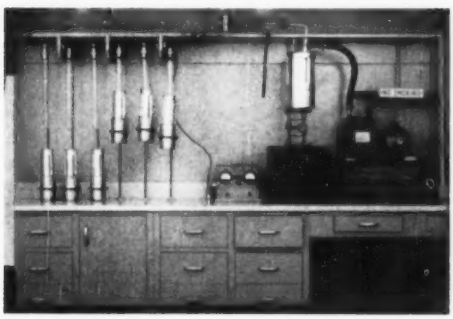
Liquid nitrogen, with a temperature of −196 C, is necessary around the trap to condense the ethylene oxide, which has a freezing point of −111 C. A Dry Ice-acetone mixture, with a temperature of −72 C, will remove the water vapor, but it is not sufficiently cold to remove the ethylene oxide, and the efficiency of the drying is markedly reduced if any of the vapor is allowed to pass over into the pump. It is to be noted that the trap can be disconnected from the rest of the unit for cleaning. By closing the stopcock *D*, the trap can even be changed during the drying procedure without losing the vacuum around the vessels. It has been considered advisable to dry the vessels at a slow rate and keep them

at a low temperature until much of the ethylene oxide hydrate and Dry Ice has passed off by the process of sublimation. To assure this, the Dry Ice mixture is kept around the vessels until the Dry Ice melts and the mixture warms up somewhat, which takes 10 to 12 hours. Then the flasks containing the mixture are lowered one at a time so that the vacuum is not reduced too much by the sudden release of a lot of water vapor from all the vessels at the same time.

The whole procedure takes from 24 to 36 hours, and one can consider that the end-point has been reached when the vacuum gauge registers 1μ to 4μ for two or three hours after all of the freezing mixture has been removed from around the vessels.

The vessel segments are stored in sterile test tubes filled with nitrogen gas and capped with a special rubber cork equipped with a lip which folds down around the outside of the tube. This was considered technically easier and safer than sealing the tube with an oxygen torch, as is done in some artery banks, and it has worked out very satisfactorily. To do this, the air is removed from the storage tube by means of a needle, which is connected to the pump and is inserted through the rubber stopper. When a vacuum has been established, nitrogen gas is allowed to flow into the tube. A complete seal is ensured by covering the stopper and the adjoining tube first with Sealstex and then with paraffin.

Fig. 2.—Photograph of the freeze-drying equipment.



Vessels from donors over 45 years of age have not been accepted, and many vessels from persons over 35 are so arteriosclerotic that they are disqualified before processing. Infection or malignant disease in the donor has not disqualified the vessels for use except when the malignancy or infection has been in close contact with the vessel. Vessels from persons with a history of syphilis or hepatitis have not been accepted, though probably the virus is destroyed by ethylene oxide. The processing of the vessel should be started within 24 hours of death, and shipment of the vessel should be carried out in isotonic saline at approximately 4 C.

During the first two years microscopic sections were made of a segment of vessel adjacent to the vessel being processed, in an effort to discover defects by such a random sampling technique. It was well recognized, however, that the vessel section so obtained did not tell everything about the remainder of the vessel, but at least it gave an approximate idea of the quality of the vessel. On the basis of these sections, 35 segments out of 425 were disqualified, mostly on the basis of advanced arteriosclerosis. Very slight arteriosclerotic changes were extremely frequent, even in vessels from donors in their 20's, and such vessels were not disqualified. A very few vessels were disqualified for changes of a nonspecific, but nonetheless suspicious, nature.

Because of the expense of obtaining histological sections and because knowledge was obtained by those studies about only small portions of the vessel, a shift has now been made to an x-ray examination of the whole vessel after it has been processed. If calcium is seen in the vessel wall on the film so obtained, the vessel is disqualified.

Results

An evaluation of the artery segments processed by the Northern California Artery Bank during the first two years of its existence seems indicated.

The Bank was established in November, 1955, to act as a processing unit for any doctor or hospital in the northern two-thirds

of California. Suitable vessels are sent to the Bank, where they are processed, and generally, if they have come from outside San Francisco, they are returned to the local community for stockpiling and use there. Because of the relatively limited supply of vessels and because of the policy of returning the vessels if so requested, the installation has served more as a processing unit than as a bank. Also, because a lot of segments have been distributed over a very large area and among many doctors and hospitals, a follow-up study is not without its problems. The only cases in which the Bank is almost sure to hear about a particular vessel is when the vessel appears defective in some way at the time of its use.

During this 24-month period, 425 vessel segments were processed, 329 were dispensed, 32 were on hand at the Bank at the end of this period, and 64 were disqualified after processing in most instances because of the histological examination or because of some technical error during processing. Of the 329 segments dispensed from the Bank, 120 are known to have been used, and 75 are on record as being stockpiled in some outlying area. Follow-up information could not be obtained on 134 segments, but some of these have without question also been used. Of the 120 segments known to have been used, 6 were merely reconstituted and, though satisfactory, were not actually used. Thus, we have follow-up information extending beyond the period of hospitalization in 114 cases, and it is with this group that the chief interest lies from the point of view of an analysis of the value and hazards of arterial homografts.

The vessels were considered satisfactory at the time of surgery in 94% of the cases and were recorded as unsatisfactory in 6%, or 7, of the cases. In the unsatisfactory group two vessels seemed extremely friable; and, unfortunately, the surgeon in each case, although he noted the defective quality while still preparing the graft, persisted in using it. In each case the vessel gave way when it had been sutured in place and the patient died. In three other cases friable vessels were found but were discarded without being used. In the sixth case the weak spot seemed confined to the region of a lumbar artery and a generalized defect was not noted. In the last vessel a crack was found in one spot and that part was discarded. The rest of the vessel was in good condition and was used.

In three of the cases in which the grafts were considered satisfactory at the time of their use, hemorrhage occurred at the suture line, in the early postoperative period, and the patients died. Whether this was due to a weakness in the graft or to the technique involved in the anastomosis cannot be determined. In another case a lumbar artery which had been ligated when the graft was sutured in place leaked several weeks postoperatively. Reoperation, with replacement of the graft, was carried out, but the patient died after the second procedure. In addition, there were two grafts which ruptured, both in patients of the same surgeon, and in one of these the rupture resulted in the death of the patient. It occurred in the case of a man who had had a femoral aneurysm removed a couple of months before and was on anticoagulant therapy because of thrombophlebitis. Postmortem, the rupture was found to have taken place in an area where there was a sharp, calcified plaque of the old aneurysm wall still in place and adjacent to the hole in the graft. It was considered that this plaque had eroded through the graft, which had not been adequately protected by surrounding it with normal soft tissue. The second rupture took place postoperatively, and the ruptured graft was removed and replaced. The patient survived. Examination of the ruptured graft revealed no reason for its rupture except that the adventitia was apparently thin or absent in the ruptured area.

One femoral artery developed an aneurysm, which was resected and replaced by a second graft, with a satisfactory result. There was thrombosis in one femoral graft where the outflow tract was considered satisfactory. Three other graft thromboses were

considered by the surgeons to be due to a proof outflow tract. No instance of sepsis in or around the graft has been reported.

As one might expect, the most frequently grafted area was the abdominal aorta, the graft usually being a bifurcation graft, and this graft accounted for 50% (56/114) of the series. Femoral grafts constituted 40% (45/114); thoracic grafts, 7% (8/114), and iliac grafts, 3% (4/114). In certain instances thoracic segments were used in the abdominal area, especially in the aneurysm cases. Certainly, the great demand was for the abdominal bifurcation and the femoral grafts.

There were 23 deaths in this series of 114 patients during surgery or at some time during the postoperative or follow-up period that were not considered to be in any way related to the graft.

Of the 35 surgeons who answered the letters and who had at one time or another made use of the grafts from the Bank, 27 stated that they preferred homografts to the synthetic segments. One stated that he liked the homografts for the smaller arteries and the plastic grafts for the larger ones, and seven stated that they preferred the synthetic grafts. By far the commonest reason given for preferring the homografts was that they were easier to work with, whereas easy availability was almost always the reason given by the surgeons choosing the synthetic grafts.

Comment

In an effort to determine more about the changes that occur in a freeze-dried artery, segments before and after the processing were studied histologically. A certain degree of fenestration in the media was noted in many of the segments studied (Figs. 3 and 4). Efforts were made to eliminate all fenestration by altering the processing methods in one way or another, and particular attention was paid to slowing down the rate of drying by keeping the vessels in the Dry Ice mixture for longer periods of time and removing the freezing mixture very gradually. No matter what method was used, many, but not all, of the vessels had a variable amount of microscopic changes. Because the alterations are so frequent and because such fenestrated vessels have been used clinically with good results, the changes are now regarded with less suspicion than was the case when they were first discovered.

Fig. 3.—Photomicrograph of vessel prior to freeze-drying.

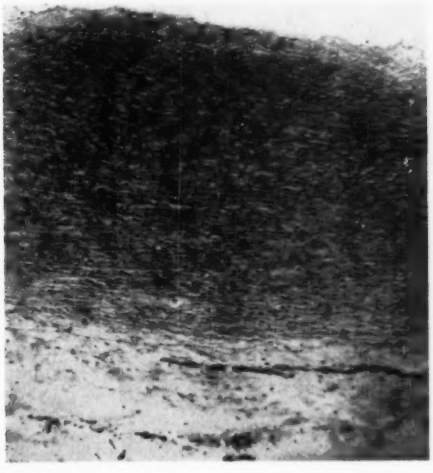


Fig. 4.—Photomicrograph of vessel following freeze-drying. Note fenestrations which result from the processing in many, but not in all, of the cases.

Attempts were made in each case in which a vessel turned out to be weak or defective to discover the nature of the defect from microscopic sections of the vessel when obtainable, from pressure tests and histological examinations of other segments from the same donor, and from a review of the cause of death of the donor and the processing methods used.

Particular attention was paid to the five vessels which seemed to have a generalized tissue weakness. The donors of three of these five vessels had met death as a result of major trauma, and it is possible that microscopic tears in the vessel walls were present which resulted in the friability noted later. Many of the vessel donors met violent deaths, however, and the vast majority of the arteries from such donors have been satisfactory. Perhaps certain types of trauma, especially the crushing injuries, may produce undesirable changes in the vessel. Microscopic examinations of the other arteries obtained from the donors supplying these defective vessels were not very specific in that the usual fenestration was noted in most of them, together with some patchy fragmentation of the elastic tissue. Pressure studies on these vessels when reconstituted revealed some gross weakening in some, but not in all, of the vessels. The weak spots occurred at the ligated intercostal or lumbar vessels.

All of the weak vessels were among those processed during the first nine months of the Artery Bank and, except for the one vessel reported cracked, the vessels during the last 15 months of this two-year period, as well as those processed since, have all been reported entirely satisfactory. The only known change that has been made in the latter part of this study period was to slow down the rate of drying somewhat and to use great care in removing the Dry Ice mixture from around the vessels so as not to allow the vapor pressure in the manifold to rise rapidly at any one time. The specimen temperature varies proportionally with the pressure in the system, and a considerable reduction in the vacuum can result in a dangerous warming of the vessel segment being dried. Whether this change has made any difference is hard to say, but, in any case, the drying is now carried out very slowly.

There are, of course, many factors in the handling of the vessels which are difficult or impossible to control completely: The careful removal and shipment of the vessels; the gentle handling and transportation of the fragile dried grafts, and the allowance of adequate time for the vessel to be reconstituted in the operating room before any attempt is made to manipulate it are but a few of the hazards above and beyond the fitness of the artery and the care in processing it.

Finally, there is the human element in the whole picture in that the two surgeons that have made the greatest use of the grafts have encountered no disasters in any way attributable to the graft. Certainly, more than one graft should be on hand for an operation requiring a graft, and if any suspicion arises with regard to the quality of the graft, it should be discarded and a second one prepared. If this had been done in two cases, deaths probably would have been avoided.

Summary

A method of processing of arterial segments by the freeze-drying technique is presented, along with a description of the equipment and the steps involved.

A follow-up study has been conducted on the 120 arterial segments known to have been used during the first two years of the existence of the Artery Bank.

Details regarding deaths and complications wholely or partially related to the homografts are presented.

It is hoped that through studies such as this the relative safety and merits of arterial

homografts and synthetic prosthesis can be gradually elucidated.

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A New Type of Vessel-Suturing Apparatus

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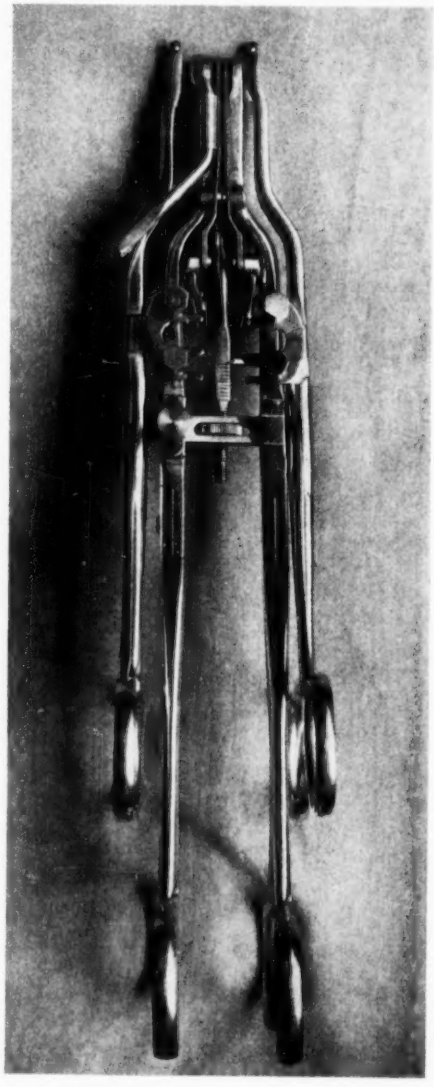
A number of shortcomings have been found with manual vessel suture. They are arising mainly from these facts: Thrombosis is not infrequent at the anastomotic portion, owing to the irregularity and injury of intima at the anastomotic line; the method requires too much time; it is difficult to anastomose small-calibered vessels.

The present paper deals with a new vessel-suture apparatus which is made to overcome these shortcomings of the manual method and to make the complicated vessel suture easy and accessible even for unspecialized surgeons. So far, the only paper on the mechanized vessel suture seems to be that of Androsov,[1] of the Soviet Union, of which I happened to learn in the course of my experimentation on this apparatus. The new apparatus is devised by my own idea, supported by my experimental evidence that if mechanical anastomosis is achieved with the vessel ends securely everted, injury of the intima is greatly reduced, and based on the principle that a surgical instrument must be simple and solid in structure.

The structure of the apparatus is shown in Figures 1 and 2. It consists of two main parts: (1) paired bushings with carrier-forceps and (2) a pair of hemostatic clamps, each of which is attached lateral to the bushing. The paired bushings are known as the "clipping bushing" and the "supporting bushing," respectively, according to their functions. Each bushing is made of two half-bushings, which are completed as a circular bushing by closing the bushing forceps. The principle of this apparatus lies in the end-to-end anastomosis of the everted intima of the two vessel ends with a line of

Fig. 1.—General view of the suturing apparatus.



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From the Second Surgical Clinic, Medical School, Kyushu University (Director: Prof. Dr. M. Tomoda).

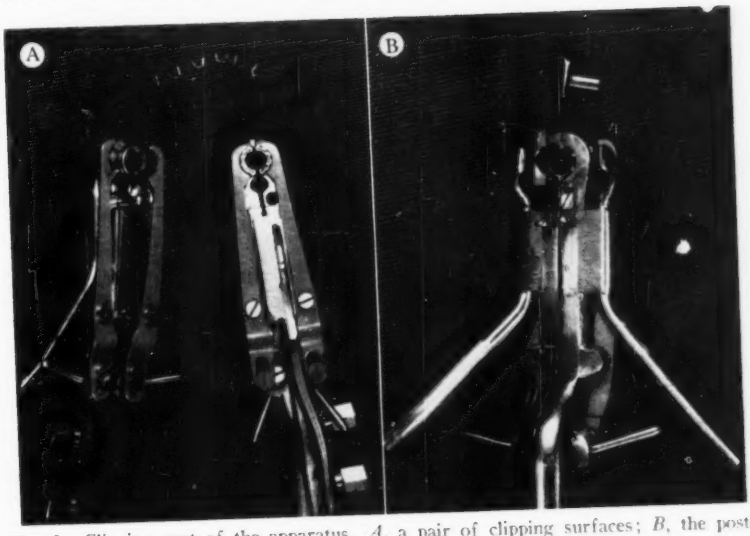


Fig. 2.—Clipping part of the apparatus. *A*, a pair of clipping surfaces; *B*, the posterior view of the clipping bushing.

U-shaped clips, which are located within the clipping bushing, with their legs directed toward the supporting bushing. Clips are driven out by a pushing-comb, which is attached to the opposite side of the clipping surface of the bushing and comes into motion by lever action. The clipping surface of the supporting bushing has many holes, corresponding in number to the clips; and when clips are driven out into the supporting bushing, their legs are bent in B-form in the corresponding holes. Clips are made of alloyed steel (22A steel), which guarantees less severe local reaction. Another accessory of the instrument is a knife-edge bar, which is wedged between the two bushings in order to avoid the destruction of intima when bushings are pressed together. A complete set of the apparatus is equipped with a dozen bushings with a series of calibers, ranging from 2.0 to 20.0 mm., each with its own carrier-forceps.

The operative procedure with this apparatus begins with the mobilization of the vessel from the surrounding tissue. The hemostat clamps are placed on each side of the future anastomosis. Half-bushings are adapted to the vessel end. The vessel end is turned inside out and fixed around the bushing with the fixing clamp. The same procedure is performed on another vessel end. Two bushing clamps are approximated and secured with the bar between them. The clipping lever is pressed, and clips are driven by the pushing-comb and run through the vessel wall. Their legs are bent in B-form in the holes of the supporting bushing, and a watertight anastomosis is completed.

Figure 3*A* shows the intimal side of the anastomosis. Clips are scarcely visible on the intimal surface, which is far better preserved with this apparatus than with the manual method. In Figure 4 the extents of intimal injury with manual and with mechanical suture are compared. This comparison is made by my original technique,[2] in which radioactive blood platelets are used to determine the adsorption of platelets onto the vessel intima. With this technique, it has been noticed that the anastomotic portion becomes transitorily, but peculiarly, adsorptive of platelets a few days after the anastomosis. However, as is shown in Figure 4, the adsorption rate is very much lower with this apparatus than with the manual-suture method; so it is quite obvious that the risk of anastomotic thrombosis is

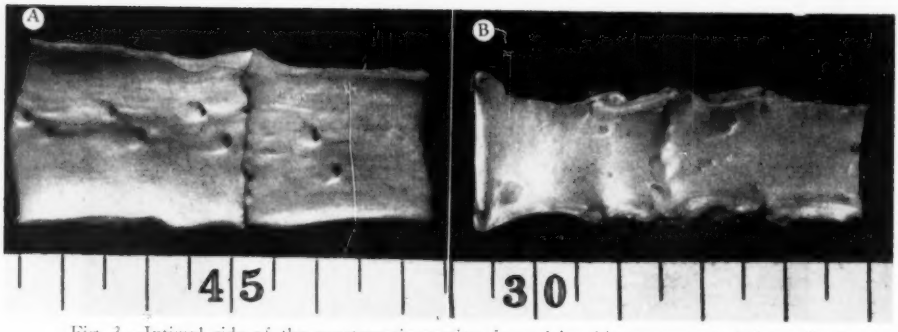


Fig. 3.—Intimal side of the anastomotic portion formed by this apparatus: *A*, immediately after mechanical suture; *B*, 80 days after mechanical suture. The anastomotic line shows no prominence but is rather concave on the intimal level.

greatly reduced following anastomosis with this apparatus. In fact, clot is scarcely visible, or, if at all, only a few tenths of that with the manual method, on the anastomotic portion with this apparatus, whereas with the manual method clot is invariably seen on the suture portion until 10 days or so after anastomosis. Thus, perfection of the mechanical anastomosis is very satisfactory also from the viewpoint of prevention of anastomotic thrombosis.

Figure 5 gives the histological picture of the anastomotic portion taken 15 days after anastomosis. It is obvious that clips induce a local reaction less severe than that to silk.

The risk of stenosis with this apparatus seems very small, as the suture line, even long after anastomosis, is concave rather than prominent with respect to the intimal level (Fig. 3*B*), whereas in the manual anastomosis the threads are exposed on the intima and, with the coverage with the newly regenerated functional intima, the line tends to be more or less prominent, so as to disturb the blood stream in case of the small-calibered vessel.

From the data of both numerous animal experiments and some clinical experience, it is shown that the apparatus prevents

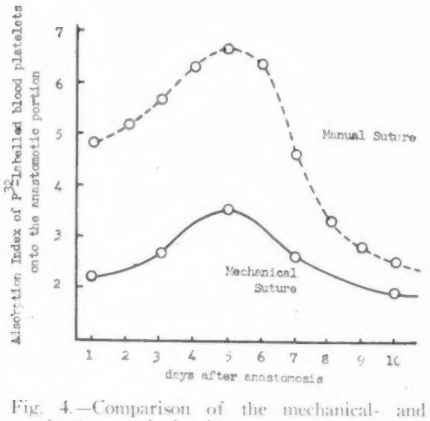
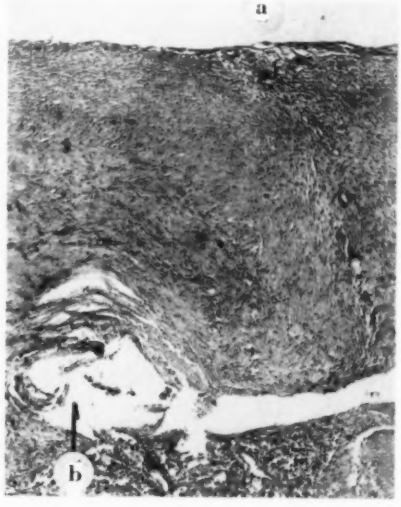


Fig. 4.—Comparison of the mechanical- and manual-suture methods with respect to the extent of adsorption of blood platelets onto the anastomotic portion.

Fig. 5.—Histological findings of the anastomotic portion 15 days after the mechanical suture. (*a*) Anastomotic line; (*b*) tissue defect resulting from removing the inlaid clip for the histological technique.



thrombosis at the line of anastomosis and permits the anastomosis or transplantation of small-calibered vessels, which has been impossible with the manual method; anastomosis is possible with a far shorter period of time than with the manual-suture method and is very easy and sure.

The characteristic features of the apparatus, especially the features which differ from those of the Russian apparatus (Gudov and associates), may be briefly mentioned. As the clip-drive mechanism, which serves the most vital function in vessel suture, is built into the bushing in a most intricate form in the Russian apparatus, one would encounter great difficulty in overhauling it. Furthermore, in order to adapt several different-calibered bushings in one apparatus, their instrument has a complicated structure, which tends to be associated with intricate handling. The Russian apparatus is undoubtedly elaborate, but this feature seems somewhat of a fault for the purpose of routine surgical employment. In my apparatus, on the other hand, the pushing-comb, which functions as the clip-drive mechanism, is easily engaged to and disengaged from the bushing, so that the cleaning or adjustment of the apparatus is very simple (Fig. 2*B*). Furthermore, the bushings of a dozen different calibers have their own carrier-forceps, so that this unit system of bushing-carrier-forceps simplifies the structure.

In conclusion, the feature of the present apparatus lies in the fact that it is made in complete accordance with the principle that a surgical instrument must be simple and solid in structure.

The practical value of my apparatus has been demonstrated in the successful results in such operative procedures as transplantation of an autogenous vein graft against a traumatic femoral arteriovenous aneurysm in a boy, against thrombosis of the femoral artery, and as peripheral anastomosis in transplanting the abdominal aorta for aortic thrombosis. A detailed account of these cases will be given elsewhere in the near future.

It is believed that my apparatus will greatly contribute to the development of cardiovascular surgery.

The Senko Medical Instrument Company, Mr. T. Aoki, president, manufactured this apparatus.

Second Surgical Clinic, Kyushi University Medical School.

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Factors Involved in Success or Failure of Arterial Grafts*

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Fig. 1.—This illustration is concerned with the role of the elastica. Besides its normal functions, its strength role and its ultimate fate in implants are discussed. The first series of curves represents a theoretical concept (Burton) of relative tensile properties of elastic tissue and collagen. One notes that there is little limitation to stretch when tension is applied to the elastic fiber short of its breaking point. Collagen, on the other hand, shows limited extension and considerably greater resistance to stress.

The next three tracings represent experimental findings on the tensile properties of an untreated artery and on tubes which are predominantly composed of either elastin or collagen. The last two materials mentioned were derived from arteries by chemical and enzymatic treatment. Their tension-elongation curves coincide remarkably well with the theoretical stress curves previously shown.

The two photomicrographs, below, deal with the fate of elastic tissue in an initially elastic implant. The first picture illustrates the early formation of a restrictive collagen envelope about an implant, while the second represents the late degeneration of elastica. Thus one can readily see that elastic *behavior* is only short-lived in originally elastic implants.

Fig. 2.—This portion of the exhibit pertains to the role of collagen, a substance which ranks high in strength among those known to man. The table shows not only that the strength of collagen is over a thousandfold that of elastica but that in fact it begins to approach the strength of steel.

To investigate the strength of collagen in an artery, we prepared a collagen tube by enzyme treatment and compared its breaking and tensile strengths with those of an unaltered vessel. The first bar graph illustrates that there is some loss in breaking strength when one compares the collagen tube with the intact artery. However, the second graph demonstrates the tensile strength of the collagen tube to be approximately equal to that of the intact artery. These data emphasize that collagen probably makes the major contribution to the strength of the arterial wall.

Despite its great strength, the manner in which the collagen fibers are disposed is of prime importance. The two photomicrographs, below, illustrate the type of weave present in fascia and in the arterial wall. It has been found that venous autografts wrapped in fascia may dilate. This can readily be understood from the picture on the left, which shows that the fascial fibers are laid down in parallel lines. Collagen disposed in this manner may fail to withstand the stresses to which it is subjected when used as an arterial substitute. On the other hand, the crisscrossing network of collagen fibers in the arterial wall provide a considerable measure of protection against the vigorous pulsatile pounding the arterial system receives during the cardiac cycle.

Fig. 3.—This figure illustrates materials that have been and are being considered as arterial substitutes. Listed are autografts, homografts, the various plastics, enzyme-treated heterografts, and heterografts. Indicated are some of their more important advantages and disadvantages.

Although autografts constitute ideal material, there are obvious limitations to their use. Homografts, on the other hand, have been employed extensively either lyophilized or after temporary storage in various media. The problems of procurement and storage, however, have necessitated extensive research into other types of prostheses.

To date, extensive investigations have been carried out on such plastics as Dacron, nylon, Teflon, Ivalon, crimped nylon, etc. Some of these materials are enjoying current acceptance, although the ideal synthetic material is yet to be discovered.

Heterografts have been found to be a poor substitute because of the undesirable tissue response that they elicit; however, they may be utilized as temporary shunts.

Enzyme-treated heterologous arteries stripped of most of their reactive proteins are also discussed. These have been shown in preliminary investigations (Rosenberg, N., and others: *S. Forum* (1955) 6:242, 1956; A. M. A. Arch. Surg. 74:89, 1957; ibid. 76:275, 1958) to elicit little if any inflammatory response as seen with the intact heterograft. Degenerative changes are minimized because of the absence of parenchymatous tissue. The response to these tubes is essentially that of a fibroplasia which invades and reinforces the implant.

Fig. 4.—This Figure is the first of two panels which illustrate some of the factors contributing to graft failure. The more important physical and biological reactions leading to necrosis, calcification, thrombosis, dilatation, and aneurysm are shown in these sections.

The introduction of any nonviable foreign tissue into the body is followed by a necrotizing reaction. Such reactions frequently predispose to calcification and chondrification. This panel illustrates these degenerative changes in homografts and heterografts.

In the absence of excessive foreign tissue (collagen tube) these reactions are minimized. This, we feel, might have contributed to the negative calcium finding, as seen in the lowermost photograph.

Fig. 5.—Thrombosis and the development of aneurysms are two important factors contributing to graft failure.

Necrosis, nature and length of the implant, hemodynamic factors, and fit are discussed in reference to thrombosis. Illustrated in the first two pictures are wrinkle thrombosis in a plastic prosthesis and the effect of a poorly fitting graft.

Aneurysms frequently result from structural weaknesses which may be inherent in the graft or acquired after implantation (degeneration). The development of a saccular aneurysm due to a focal defect and the induction of an aneurysm by intentional proximal constriction are shown in the last two pictures.

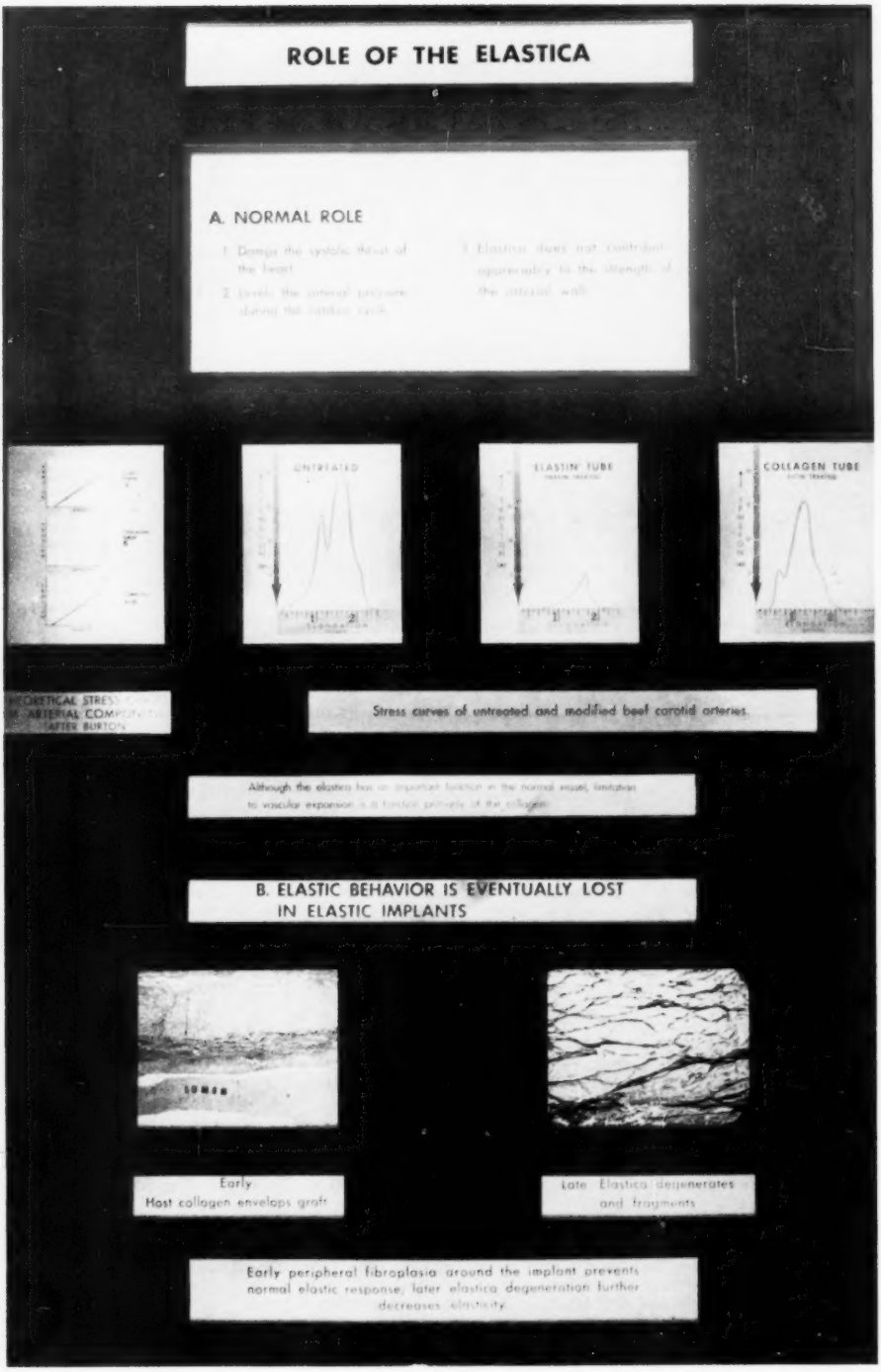
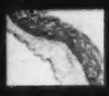

ROLE OF THE ELASTICA
A. NORMAL ROLE
UNTREATED
ELASTIN TUBE
COLLAGEN TUBE
Stress curves of untreated and modified beef carotid arteries
B. ELASTIC BEHAVIOR IS EVENTUALLY LOST IN ELASTIC IMPLANTS
Early
Host collagen envelops graft
Late Elastica degenerates and fragments
Early peripheral fibroplasia around the implant prevents normal elastic response; later elastica degeneration further decreases elasticity

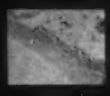
Figure 1

ROLE OF THE COLLAGEN

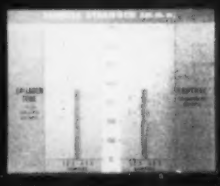
A. STRENGTH OF COLLAGEN

TENSILE AND ELASTIC PROPERTIES OF VARIOUS MATERIALS

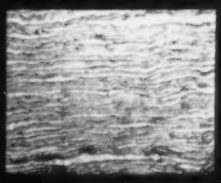




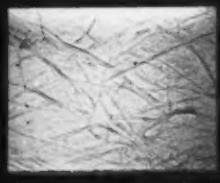
These graphs show that collagen is responsible for a major portion of the strength of the arterial wall. It is interesting to note that an artery can be reduced to a collagen tube without loss of tensile strength.



B. IMPORTANCE OF WEAVE



COLLAGEN PATTERN IN FASCIA
(rabbit abdominal aponeurosis)



COLLAGEN PATTERN IN ARTERY
(beef carotid adventitia)

In the arterial wall the collagen weave is more intricate with criss-crossing of fibers than in fascia, providing strength in all directions.

Figure 2

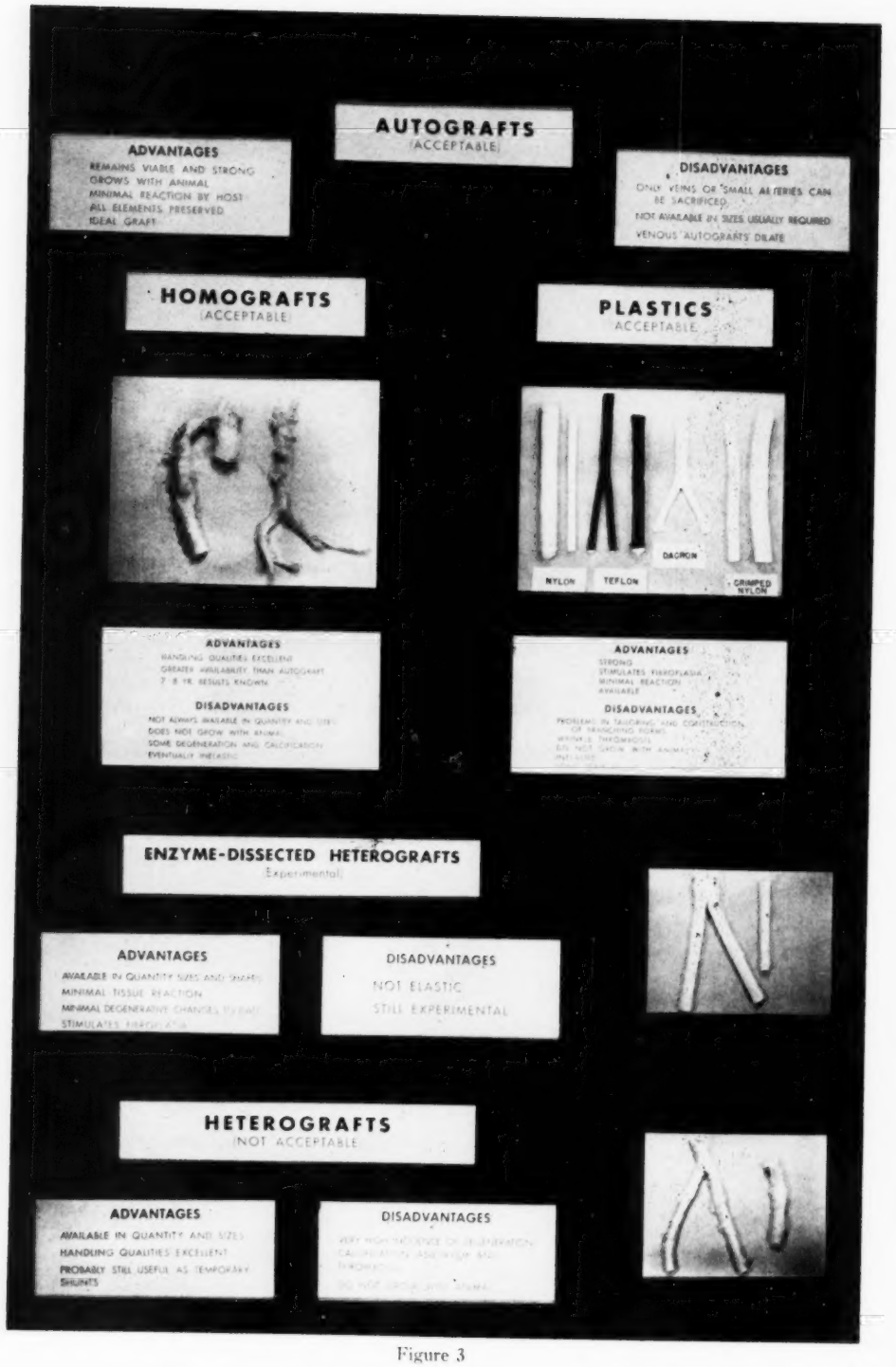
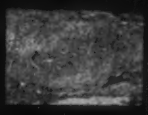

AUTOGRAFTS
(ACCEPTABLE)
ADVANTAGES
REMAINS VIABLE AND STRONG
GROWS WITH ANIMAL
MINIMAL REACTION BY HOST
ALL ELEMENTS PRESERVED
IDEAL GRAFT
DISADVANTAGES
ONLY VEINS OR SMALL ARTERIES CAN BE SACRIFICED
NOT AVAILABLE IN SIZES USUALLY REQUIRED
VENOUS AUTOGRAFTS DILATE
HOMOGRAFTS
(ACCEPTABLE)
PLASTICS
ACCEPTABLE
DACRON
NYLON
TEFLON
CRIMPED NYLON
ADVANTAGES
HANDLING QUALITIES EXCELLENT
GREATER AVAILABILITY THAN AUTOGRAFT
7 - 8 YR. RESULTS KNOWN
DISADVANTAGES
NOT ALWAYS AVAILABLE IN QUANTITY AND SIZE
DOES NOT GROW WITH ANIMAL
SOME DEGENERATION AND CALCIFICATION
EVENTUALLY INELASTIC
ADVANTAGES
STRONG
STIMULATES FIBROPLASIA
MINIMAL REACTION
AVAILABLE
DISADVANTAGES
ENZYME-DISSECTED HETEROGRAFTS
Experimental
ADVANTAGES
AVAILABLE IN QUANTITY SIZES AND SHAPES
MINIMAL TISSUE REACTION
MINIMAL DEGENERATIVE CHANGES EVENTUALLY
STIMULATES FIBROPLASIA
DISADVANTAGES
NOT ELASTIC
STILL EXPERIMENTAL
HETEROGRAFTS
(NOT ACCEPTABLE)
ADVANTAGES
AVAILABLE IN QUANTITY AND SIZES
HANDLING QUALITIES EXCELLENT
PROBABLY STILL USEFUL AS TEMPORARY SHUNTS
DISADVANTAGES

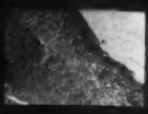
Figure 3

A. NECROSIS

1. Leads to increased cellular reaction.
2. Delays fibroblastic and capillary invasion.
3. Predisposes to late calcification. Metaplastic bone and cartilage formation may be seen.
4. Leads to increased local output of thromboplastic substances with early thrombosis.
5. Prolongs the period during which complications can occur.



NECROSIS

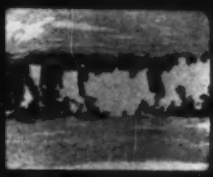


CELLULAR REACTION

B. CALCIFICATION

1. HOMOGRAFT

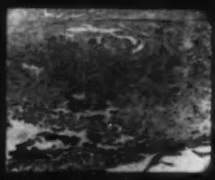
Occurs mainly in the media at the site of smooth muscle degeneration or later in relation to degenerating elastic fibers.



LATE ELASTICA DEGENERATION AND CALCIFICATION

2. HETEROGRAFT

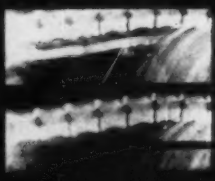
The reaction here is similar to that seen with homografts, but with greater severity and possibly greater frequency.



METAPLASTIC CHONDRIFICATION IN HETEROGRAFT

3. ENZYME-DISSECTED HETEROGRAFT

No radiological or autopsy evidence of calcification after observation period up to 18 months.



EIGHTEEN MONTHS OLD IMPLANT

Figure 4

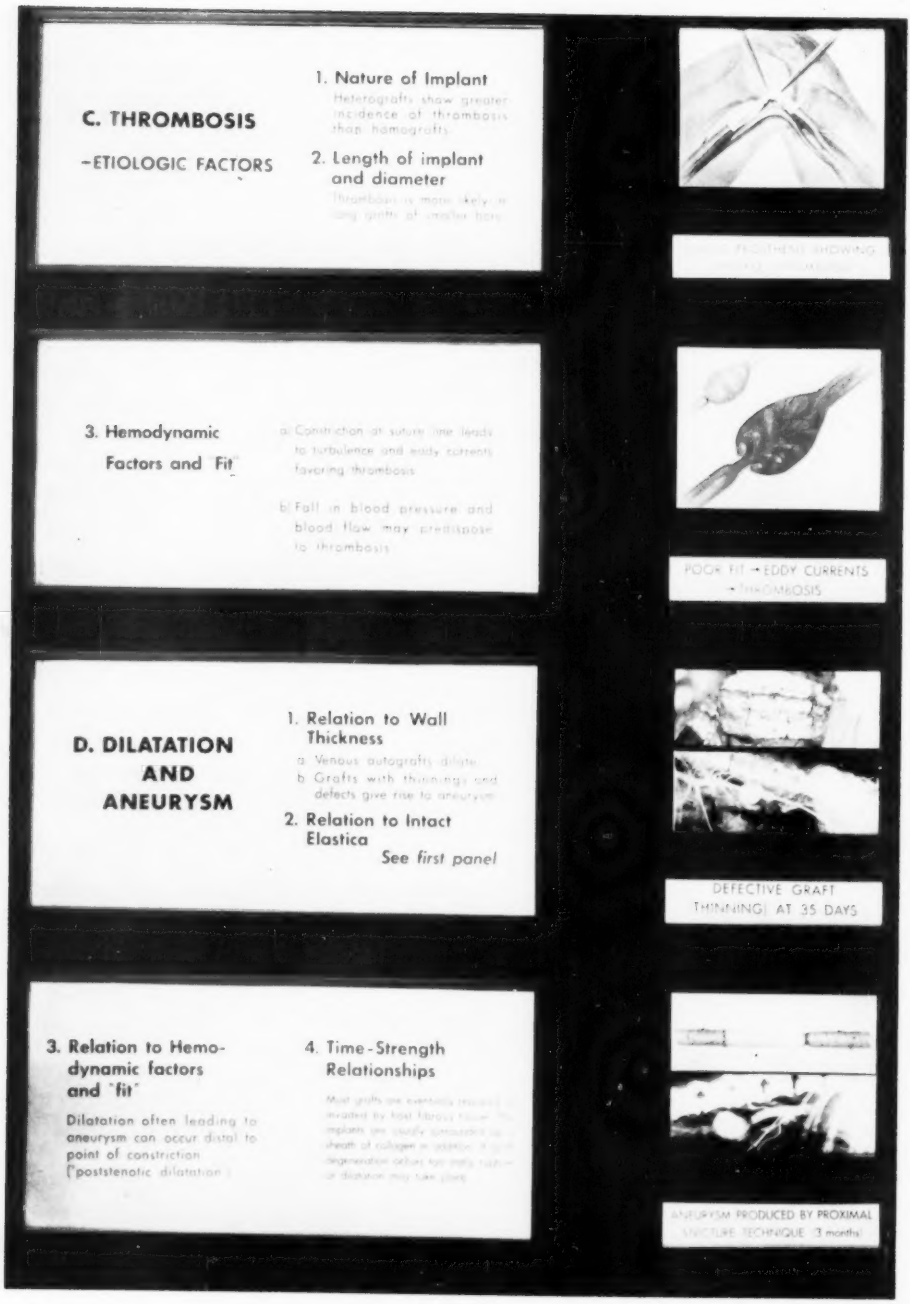

C. THROMBOSIS
-ETIOLOGIC FACTORS
1. Nature of Implant
Heterografts show greater incidence of thrombosis than homografts
2. Length of implant and diameter
Thrombosis is more likely in long grafts of smaller bore
3. Hemodynamic Factors and Fit
a. Constriction at suture line leads to turbulence and eddy currents favoring thrombosis
b. Fall in blood pressure and blood flow may predispose to thrombosis
POOR FIT → EDDY CURRENTS → THROMBOSIS
D. DILATATION AND ANEURYSM
1. Relation to Wall Thickness
a. Venous autografts dilate
b. Grafts with thinnings and defects give rise to aneurysm
2. Relation to Intact Elastica
See first panel
DEFECTIVE GRAFT THINNING AT 35 DAYS
3. Relation to Hemodynamic factors and "fit"
Dilatation often leading to aneurysm can occur distal to point of constriction ("poststenotic dilatation")
4. Time-Strength Relationships
ANEURYSM PRODUCED BY PROXIMAL STRICTURE TECHNIQUE (3 months)

Figure 5

Johnson & Johnson Research Foundation.

Aneurysm of Aortic Homograft with Rupture into the Duodenum

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Introduction

Massive gastrointestinal hemorrhage is a serious and often fatal condition, requiring the joint efforts of the physician and the surgeon. Prompt recognition of uncontrolled hemorrhage warrants the immediate attendance of a surgeon. Although the great majority of gastrointestinal hemorrhages are due to peptic ulcer, esophageal varices, carcinoma of the stomach, and gastritis, there is a small group of cases for which surgery is mandatory. Rupture of an aortic aneurysm into the gastrointestinal tract has infrequently been reported, and only recently has a patient with one survived.[20] The occurrence of an aneurysm developing in an aortic homograft with subsequent rupture into the gastrointestinal tract has not previously been reported, to our knowledge. The following report represents such a case with survival.

Report of a Case

The patient, aged 70, was first admitted to Seaside Memorial Hospital on March 5, 1958, at 6:50 p. m. Four hours prior to admission the patient had abdominal discomfort, followed by vomiting. There was no blood in the vomitus. Shortly afterward he had four large bloody bowel movements and was sent to the emergency room by his physician. Blood pressure on arrival was 118/70 and hemoglobin 12.7 gm. %. He was transferred to the ward, where he had another large bloody bowel movement and the blood pressure dropped to 80/40. Transfusions were started at 8:30 p. m.

The past history revealed that in December, 1954, the patient had an aortic aneurysm resected by Dr. O. C. Julian, of Chicago, and a homograft inserted (Fig. 1).

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From the Medical and Surgical Services of the Seaside Memorial Hospital.

Examination on admission revealed that the patient was an elderly man, mentally clear but sleepy. His skin and conjunctivae were pale. The heart rate was 100, with regular rhythm; blood pressure was 80/40. The abdomen was flat. The aortic pulsations were palpable, and there were good femoral pulsations on both sides.

At 9:30 p. m. he had a large hematemesis; a Levin tube was passed and bright red blood aspirated. Further rapid transfusions were started by cut-down, and the patient was scheduled for emergency surgery. Operation was begun at 11:15 p. m.

The stomach and small bowel were found filled with blood. No lesion could be felt in the stomach or duodenum. The aortic homograft felt hard. A cherry-sized aneurysm was present in the first portion of the graft. Gastrotomy was performed, and bright red blood could be seen coming from the duodenum. There was no evidence of ulceration in the stomach or duodenum. From within, the aneurysm could be felt thinning the third portion of the duodenum, with the sensation of a jet of blood against the finger. There were many adhesions of the ileum and jejunum to the homograft. These were dissected with great difficulty until, finally, the homograft could be visualized. The third portion of the duodenum was densely adherent to the aneurysm, and when it was dissected free, the source of hemorrhage was obvious. A 1 mm.-sized hole was present in the aneurysm, which had penetrated into the duodenum. Blood was spurting briskly from this hole. The patient's aorta just distal to the renal arteries was mobilized and a Potts clamp placed across the aorta at this level. The homograft was dissected out for about 2 in., at which point it became fused with the vena cava and common iliac veins. This portion of the homograft was then removed with a small cuff of the patient's proximal aorta. The distal homograft was ligated with a silk tie. An Edward-Tapp braided nylon graft* was inserted into the defect. The common iliac arteries were too involved in scar tissue to be anastomosed; so the external iliac arteries were used. Good blood flow was obtained down both femoral arteries. An 18 in. segment of ileum was resected because of serosal trauma in dissecting it from the homograft.

Fig. 1.—Intravenous pyelogram, Dec. 18, 1954. The abdominal aortic aneurysm is outlined by a layer of calcium.

The defect in the duodenum was closed transversely with an interrupted silk suture. The gastrotomy was closed in one layer with interrupted silk suture. One Penrose drain was placed to the homograft, and the wound was closed.

The patient received 7500 cc. of blood just prior to and during surgery. On the following morning the hemoglobin was 16.5 gm. % and the hematocrit 44%. A moderate amount of blood continued to drain from his stab wound drain for 36 hours, and he was given 500 cc. more blood on March 7. On this day, his hemoglobin was 13.4 gm. % and his hematocrit 38%. Postoperatively he did well. The pulsations in the right leg were present down to and including the posterior tibial artery. In the left leg no pulsation could be felt below the superficial femoral artery. The skin color of both legs was good, although the right leg was warmer than the left. (Later the patient told us that this condition had been present for the past year.) On the fourth postoperative day the Levin tube was removed and the patient started on oral feedings. He was made ambulatory on the 5th day and discharged home on the 11th postoperative day.

Since his discharge from the hospital the patient has done well. His pulses have remained strong, and he is slowly gaining weight.

Pathologic Report (Fig. 2).—The portion of the aortic graft removed measures 60 mm. in length and has an average diameter of 35 mm., including the surrounding fibrofatty tissue. At the proximal line of resection sutures are still present. Six millimeters distal to the proximal line of resection the lumen narrows from 20 to 8 mm. in diameter. There are an extensive white plaque and yellow atheromatous thickening of the aortic graft wall. At the distal line of resection the diameter is 10 mm., and there is extensive yellow plaque formation. There is a small perforation in the aortic wall, measuring 1 mm. in diameter.

Fig. 2.—The retouched line demonstrates the perforation in the aneurysm. The narrowed anastomosis can be seen in the center of the proximal end of the specimen. From a Kodachrome slide.

Comment

In a consecutive series of 28,400 autopsies reviewed by Kane, Meyer, and Kozoll,[11] arterial aneurysm rupturing into the gastrointestinal tract was the fourth commonest cause of fatal hemorrhage. In April, 1958, Voyles and Moretz[20] reported an instance of an aortic aneurysm rupturing into the duodenum with hematemesis of approximately 500 cc. The patient was given 500 cc. of whole blood at a local hospital before being transferred to the Medical College of Georgia. An upper gastrointestinal series did not reveal any esophageal varices, and the patient was explored approximately eight hours after admission. A large abdominal aneurysm which had ruptured into the third portion of the duodenum was observed. It was resected and replaced with a combined polyvinyl formalinized (Ivalon) and Teflon graft. On the 34th postoperative day the patient developed abdominal pain; peritoneal tap revealed dark blood, and reexploration was done. A small leak was found at the anastomosis between the graft and the left common iliac artery. This leak was easily repaired; however, on the third postoperative day, the patient suffered a cerebral vascular accident and died two days later.

On reviewing the literature, the authors[20] found 63 instances of aortic aneurysm rupturing into the gastrointestinal tract, and there was no instance in which the lesion was attacked surgically. In a great majority of these patients there was a sufficient interval between onset of bleeding and death to allow operative attack on the lesion had the diagnosis been suspected and immediate surgery undertaken.

Degenerative changes in arterial and aortic homografts have been reported by

various authors.[1-5,7,9,12,19] In some instances occlusion and leaks at anastomotic sites have required removal of the original graft and replacement with a synthetic prosthesis or an additional homograft. Dilatation of aortic homografts has rarely been reported,[3,5,7,16,18] and in only two instances has the graft ruptured. In 1957 Susman and Palmer [16] reported a case of an abdominal aneurysm which had been bypassed and excluded from the circulation, the defect being replaced by a homograft. Eleven weeks postoperatively the patient had severe abdominal pain with signs of hemorrhage. He was explored two days later, and clots of blood were found in the peritoneal cavity. The clots were removed, and no bleeding area could be found. The abdomen was closed. The patient died suddenly two days later, and at autopsy two saccular aneurysms were seen on the anterolateral surface of the graft. The aneurysms seemed to arise at the origin of an aortic branch and were surrounded by hematoma, but no definite rupture could be found. The suture lines were intact.

Gwathmey and Thompson [7] resected a localized aneurysmal dilatation in a homograft that had been used to replace a fusiform aneurysm of the lower part of the thoracic aorta 12 months previously. The new aneurysm was excised and a plastic graft successfully inserted. In this case, the first homograft had been divided in its central portion and a segment removed, because of its being too long when first inserted. In March, 1958, Jamplis and associates [10] reported fatal rupture in an aortic homograft. The patient had an abdominal aneurysm resected and replaced by a homograft, followed 11 months later with pain in the back. Surgical exploration was undertaken and a large aneurysm at the top of the homograft found. They considered it impossible to resect, and nothing further was done. The patient died three weeks later, with rupture of the aneurysm.

In the case presented the homograft and aneurysm were resected and replaced successfully with a nylon graft.[6] No previous successful replacement has been found on reviewing the literature.

Summary

A case of rupture of an aneurysm in an aortic homograft is reported. The presenting symptom was massive upper gastrointestinal hemorrhage. No previously reported case has been found on reviewing the literature. Early aggressive treatment of continued massive upper gastrointestinal hemorrhage is urged.

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Aneurysm of the Splenic Artery

W. C. SHANDS, M.D., and J. HARVEY JOHNSTON Jr., M.D., Jackson, Miss.

Aneurysms of the splenic artery are rare lesions, the incidence being 0.038% in collected autopsy series.[1] Hill and Inglis[8] found that 245 cases had been reported by Jan. 1, 1955. Since their publication, 22 additional proved cases have been reported in the world literature.[2-7,9,11-13,15-18] In a collective review by Owens and Coffey,[10] published in October, 1953, the average age incidence was found to be 48 years, and there were twice as many women as men with aneurysms of the splenic artery. The occurrence in pregnant women, particularly in the last trimester of pregnancy, has been noted frequently. The following case report of a patient with five saccular aneurysms of the splenic artery which were successfully resected is reported.

Report of a Case

A 58-year-old white woman was admitted to the St. Dominic-Jackson Memorial Hospital on June 24, 1956, with a chief complaint of pain in the left upper quadrant of the abdomen. Approximately 30 years prior to admission, during the patient's last pregnancy, she had noted left upper quadrant distress, and subsequent to this pregnancy she was told that she had an enlarged spleen. Ten years prior to admission the patient had a toxic substernal adenomatous goiter removed elsewhere. At the time of her hospitalization for thyroidectomy, she was found to have diabetes mellitus, and she had followed a diabetic diet and taken 40 units of protamine zinc insulin daily since that time. Three months before admission, the patient developed a severe pulling type of pain across the upper abdomen, and she had much soreness, particularly in the left upper quadrant of her abdomen. She had had no jaundice, and there was no history of any bleeding tendency. In the three months prior to admission the patient had had a 10 lb. weight loss.

On physical examination, her blood pressure was 140/72. Abnormal physical findings were limited to the abdomen. The patient had a markedly enlarged spleen, felt 1 handbreadth below the left costal margin. No thrill or bruit was detected in the abdomen. Peripheral arterial pulsations were entirely normal. The initial laboratory data revealed a hemoglobin of 12.4 gm. %, with a red cell count of 4,380,000 and a hematocrit of 39 vol. %. White blood cell count was 5100, with normal differential and platelet counts. The serological test for syphilis was negative. Urinalysis was negative. Serum amylase was 54 mg. %, and the prothrombin time was 82% of normal. The fasting blood sugar was 330 mg. %. Teleoroentgenograms were obtained. A scout film of the abdomen (Fig. 1) revealed that the splenic shadow was considerably enlarged. There was dilatation about the region of the splenic artery with several large areas of calcification. One area of calcification was seen in the right upper quadrant and was thought to represent calcification in a branch of the hepatic artery. Intravenous pyelography revealed a normal urinary tract. Barium enema examination was negative. Cholecystograms were negative, and upper gastrointestinal examination revealed an extrinsic pressure defect on the postero-

Fig. 1.—Scout film of the abdomen, showing an enlarged splenic shadow and concentric calcifications in the region of the splenic artery.

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From the Surgical Clinic.

Fig. 2.—Extrinsic pressure defect on the posterolateral wall of the stomach from aneurysm of the splenic artery.

lateral wall of the stomach, believed to be due to adjacent aneurysmal dilatation of the splenic artery (Fig. 2).

A preoperative diagnosis of splenomegaly with aneurysm of the splenic artery was made. The patient was operated upon on June 28, 1956, through a left thoracoabdominal incision in the eighth intercostal space and extending past the midline of the abdomen. A markedly enlarged spleen was found, with numerous adhesions posteriorly. These were divided by sharp dissection. The splenic vessels were clamped and ligated at the hilus. The spleen was delivered into the wound. The splenic artery was found to contain five separate aneurysms, and these were intimately bound to the superior surface of the body and tail of the pancreas. Dissection was extremely difficult, but the proximal splenic artery at the celiac axis was finally identified, doubly ligated, and divided. The entire aneurysmal mass was then removed with the spleen, including a portion of the pancreatic capsule. There was profuse bleeding from numerous points. The bleeding was controlled by packing and then by suture ligatures. The patient received 3500 cc. of blood during the procedure. Drains were left through stab wounds in the abdomen down to the pancreatic bed, and an intercostal catheter was employed. The patient's postoperative course was smooth, and she has remained well, 18 months postoperatively.

Pathological examination revealed five saccular aneurysms of the extremely tortuous splenic artery (Fig. 3). The largest aneurysm measured 40×35×34 mm., and half of its sac was filled with a clot. The wall of the artery and the aneurysmal sacs were extensively calcified. The spleen (Fig. 4) weighed 900 gm. and showed dilated blood vessels on cut surface. Microscopic section of the spleen showed an essentially normal structure except for thickening of the blood vessel walls. Sections of the aneurysm showed thickening of the intima, and large areas of the media were calcified. In other areas, there was an increase in fibrous tissue, and

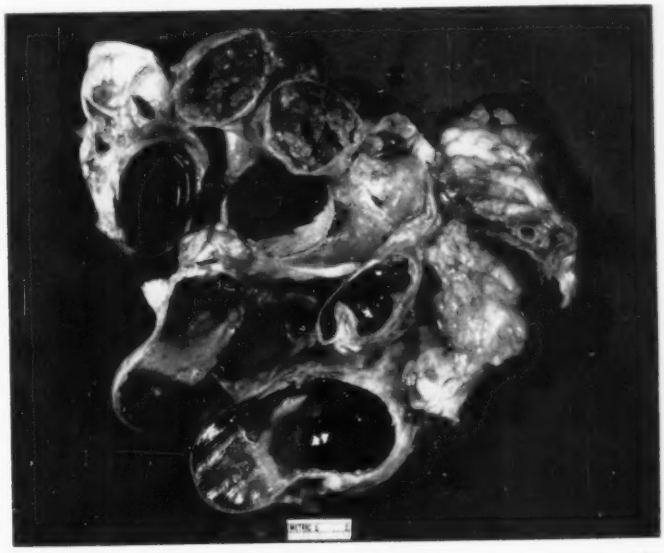

Fig. 3.—Five saccular aneurysms of the splenic artery in cross section.

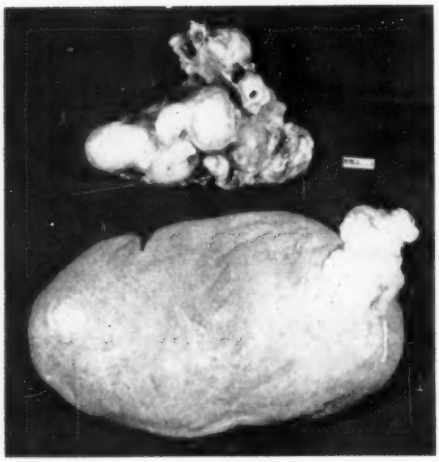

Fig. 4.—The 900-gm. spleen with the aneurysmal mass.

in one of these areas there were lymphocytes and bone formation. The final diagnoses were saccular aneurysms, multiple, of the splenic artery, heteroplastic bone formation of splenic arterial aneurysm, and chronic congestive splenomegaly.

Comment

Clinical Aspects.—This patient presented several features which are quite characteristic of aneurysms of the splenic artery. The onset of splenomegaly in this patient was at the time of the patient's last pregnancy, and these aneurysms are known to occur frequently in pregnant women. Splenomegaly may arise during pregnancy and may cause changes in the splenic arterial wall which predispose to aneurysm formation. Splenomegaly was present in 45% of 161 cases in the collected review of Owens and Coffey.[10]

Several observers have reported additional palpable left upper quadrant tumor masses separate from the spleen, and in some cases a bruit has been heard or a thrill has been felt. The latter findings were not present in this patient, possibly owing to the heterotopic bone formation with extensive calcification.

The diagnosis was made in this patient on the basis of the scout film of the abdomen and the upper gastrointestinal series. The scout film revealed diagnostic calcification, which was further confirmed by the indentation of the posterior wall of the stomach by the large aneurysm. Translumbar aortography has been helpful in the diagnosis of obscure splenic arterial aneurysms but is, of course, not indicated in the presence of calcification and extrinsic pressure defects, easily demonstrable on x-ray of the stomach.

The patient's presenting symptom was of severe left upper quadrant pain of several months' duration. Thrombosis of one of the saccular aneurysms was encountered at the time of surgery. Rupture of a splenic arterial aneurysm may present as an acute abdominal crisis associated with internal hemorrhage. Owens and Coffey reported two-stage or double rupture of splenic aneurysms in 21% of 204 cases. The second hemorrhage developed usually within 48 hours of the primary incident.

Pathology.—The etiologic factors which are associated with splenic artery aneurysms include arteriosclerosis, mycotic aneurysms associated with subacute bacterial endocarditis, congenital aneurysms, and those associated with portal hypertension, trauma, or syphilis.

This patient exhibited marked evidence of arteriosclerosis in the splenic artery; in addition, the spleen, which was quite large, exhibited the histologic appearance of congestive splenomegaly. In the series of Owens and Coffey 20% of the patients showed evidences of portal hypertension. In this patient, the only suggestion of portal hypertension was in the spleen itself. The small aneurysm of the hepatic artery present in this patient has not become symptomatic.

Results of Treatment.—The treatment is surgical removal, and in most instances splenectomy has been performed, in addition to removal of the splenic artery aneurysms. Owens and Coffey, in 1953, reported 33 cases in which the patients survived operation for splenic aneurysm. The mortality rate in cases operated upon before rupture of the aneurysm was found by these authors to be 29%. Since this report 13 additional cases of successful resection have been re-

ported. However, even with a planned approach, technical difficulties of the operation may be extremely great.

Ten cases have survived operation for a ruptured splenic aneurysm, but the collected mortality was 76% in the report of Owens and Coffey. The operation for splenic aneurysm before rupture now offers a good prognosis, while after such a catastrophe the risk remains high. Accordingly, it is well to think of an aneurysm of the splenic artery in the differential diagnosis of obscure left upper quadrant pain and in the differential diagnosis of splenomegaly and obscure gastrointestinal hemorrhage. Calcification of the splenic artery aneurysm on scout film is of great diagnostic assistance, and translumbar aortography may be very helpful in those cases in which the aneurysm has not calcified. This patient is the second reported patient with diabetes mellitus and splenic artery aneurysm. In this patient, there was evidence at the time of surgery of marked compression of the body and tail of the pancreas. The diabetic status of this patient has been unchanged subsequent to splenectomy and removal of the aneurysm of the splenic artery.

Summary

A 58-year-old white diabetic woman presented with pain in the left upper quadrant of the abdomen of three months' duration. She had been known to have an enlarged spleen for 30 years, since her last pregnancy.

Scout film of the abdomen disclosed calcified aneurysms of the splenic artery, and gastrointestinal series disclosed a pressure defect on the posterior wall of the stomach. The spleen and five saccular aneurysms of the splenic artery were removed through a left thoracoabdominal incision.

The patient has remained asymptomatic since this operation, 18 months ago.

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Reaction of Dog Artery and Brain to Latex

Further Laboratory Studies Related to Surgery of Intracranial Aneurysms

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In a previous study [1] several plastic substances and natural latex were tested as agents that could be applied to blood vessels to promote fibrosis and thereby strengthen the vessel wall. Of these substances, natural Hevea latex seemed the most satisfactory. Because of its white color, even distribution over the entire surface could be assured under direct vision. With acidification of the vessel surface with 0.5% acetic acid, latex applied over the surface "set" in about two minutes. The inflammatory response and fibrosis from latex seemed to be of the desired intensity.

In the present series of animal experiments an attempt has been made to determine the feasibility of applying latex to the cerebral vessels of man. Tests were made (1) to observe further vessel thickening and perivascular fibrosis; (2) to determine the reaction of central nervous tissue to latex; (3) to observe handling properties of latex in the immediate control of fresh arterial hemorrhage, and (4) to determine a method of sterilization of latex.

Experimental Method

Twenty-two adult mongrel dogs were used and later killed at periods varying from three weeks to six months. With ether anesthesia and aseptic surgical technique, latex was applied to 5 femoral arteries and to the cervical portions of 10 carotid arteries. Latex was applied to the cerebral surface 12 times, to the pontine surface once, to the spinal cord surface once, and to the cerebral white matter in brain wounds four times. Natural liquid latex was applied to some vessels without acidification and to others after applications of 0.5% acetic acid solution to hasten solidification of latex. Absorbable gelatin sponge U. S. P. (gelatin foam) or oxidized cellulose cotton was soaked in latex and applied as a cohesive cuff around six peripheral vessels. Pledgets of absorbable gelatin sponge or oxidized cellulose soaked in latex were applied over the cerebral convexities eight times. Four experimental brain wounds were made by subpial suction removal of 1 sq. cm. areas of cortex and the wounds packed with either absorbable gelatin sponge or oxidized cellulose soaked in latex.

The reaction of four peripheral vessels to irradiated latex was compared with the reaction to heat-sterilized latex.

All of the latex used in these studies had been placed in containers in an autoclave at 240 F for one hour and then transferred to small sterile glass bottles and sealed.* Routine bacterial and fungus cultures were made of several bottles selected at random, some of which had been prepared as long as one year previously. Two bottles, in addition to heat sterilization, received 5.6 mega-rep of gamma radiation from a 3000-curie Co^{60} source.† Additional bacterial studies were made on the two irradiated specimens.

Experimental Results

Physical Properties of Latex.—Latex applied to artery adventitia or arachnoid could be spread over the surface in a thin coat as a white, moderately viscous liquid, similar to paint. The liquid latex became tacky and ceased to flow in two minutes and could not be wiped from the surface in five minutes. Acidification of the surface with

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* Latex was supplied by L. B. Sebrell, Director, Research and Development Department, International Latex Corporation, Dover, Del.

† Use of this source and technical advice were given by Dr. Richard Glass, Physical Sciences Division, Stanford Research Institute, Stanford, Calif.

0.5% acetic acid before application of latex caused the latex to solidify in about one-half the time. Latex exposed to 5.6 megarep of gamma radiation appeared no different in color or viscosity, but hardened in two to three minutes.

Absorbable gelatin sponge, oxidized cellulose gauze, and oxidized cellulose cotton soaked in latex, if held in open air for one to two minutes, could be wrapped about vessels as a cohesive cuff, but such a cuff did not stop bleeding from a laceration in the arterial wall.

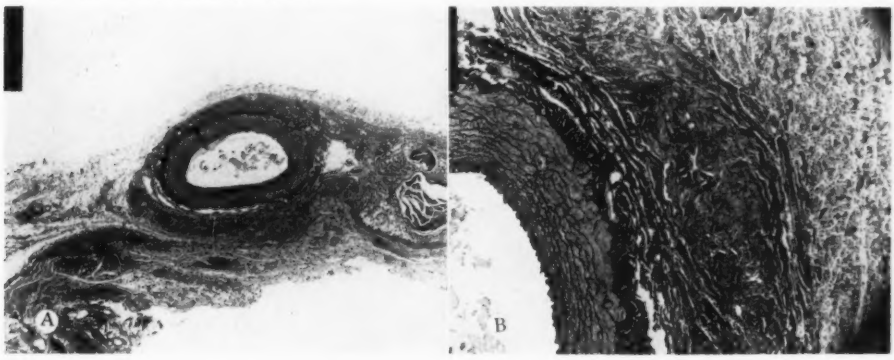
Gross Findings.—There was no suppuration in any of the latex-treated wounds. The only instance of faulty wound healing was in the presence of clear, yellow subgaleal fluid in one animal.

Peripheral vessels painted with a thin coat of latex, when dissected after three weeks, appeared little different from vessels merely exposed and not painted. The gross form of the vessel was easily identified and could be dissected from surrounding muscles without difficulty. However, a thin, adherent, opaque fibrous covering could not be separated from adventitia. Where a latex-soaked oxidized cellulose or absorbable gelatin sponge pledget had been wrapped about the vessel, a hard, thick, whitish-yellow cuff containing enmeshed fragments of solid latex fixed the vessel to adjacent tissue. In all instances the distal portion of the vessel, when divided, bled freely.

One month after painting the arachnoid over the cerebral cortex there was little or no visible dural or arachnoidal thickening, and adhesions were no greater than in control wounds. Similar lack of grossly visible reaction and of dense adhesions was observed after coating the cerebellar hemisphere, pons, and lower cranial nerves, and over the spinal cord after injecting liquid latex into the spinal subdural and subarachnoidal spaces. Latex-soaked absorbable gelatin sponge or oxidized cellulose pledgets implanted in the cranial subdural space caused slight indentation of the cortex from the firm fibrous mass and moderately dense dural adhesions. The findings were the same in instances of brain wounds made by suction removal of cortex.

Microscopic Findings.—After three weeks vessels painted with either heat-sterilized latex or irradiated latex showed an even, moderately thick zone of proliferating fibroblasts and connective tissue (Fig. 1). The surrounding zone of fibrosis was much thicker in those specimens wrapped with latex and oxidized cellulose or absorbable gelatin sponge (Fig. 2). Acute inflammation and necrosis were not evident. No neoplastic tissue has been observed in sections after six months. Intimal prolifera-

Fig. 1.—Fibrosis about carotid artery one month after application of irradiated latex. *A*, Weigert's elastic fiber-Van Gieson stain; ×16. *B*, Weigert's elastic fiber-Van Gieson stain; reduced to 58% of mag. ×68.



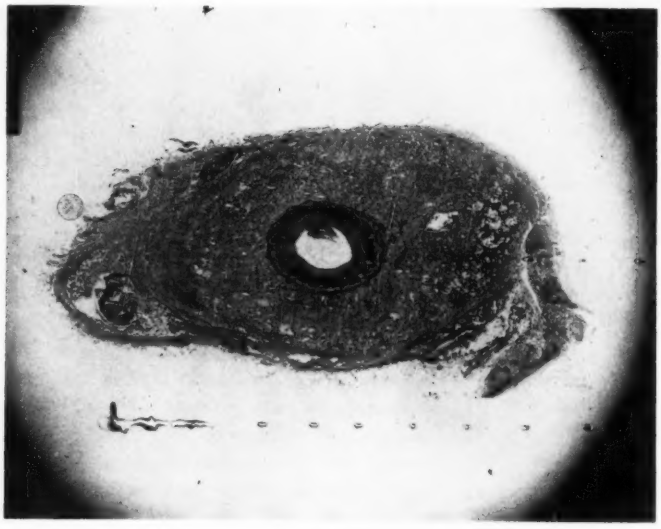


Fig. 2.—Adventitial fibrosis and thickening, carotid artery, one month after wrapping in absorbable gelatin sponge (gelatin foam) with latex spread over surface. Weigert's elastic fiber-Van Gieson stain; reduced to 86% of mag. ×8.

tion or thrombus formation has not been observed in any of the specimens.

Latex applied over the arachnoidal surface of the brain produces very minimal reaction in the meninges (Fig. 3). After three months the experimental and control specimens appear the same. The degree of meningeal reaction appears to depend upon the thickness of the application; a thin coat applied over exposed cortex leaves no visible reaction, but latex injected into the confines of the spinal subarachnoid space over the cord leaves a closely adherent fibrous tissue layer, equal in thickness to that of dura (Fig. 4). Absorbable gelatin sponge soaked in latex leaves a thick, dense connective tissue layer between the meninges (Fig. 5).

Even beneath the thick fibrous mantle caused by latex and absorbable gelatin

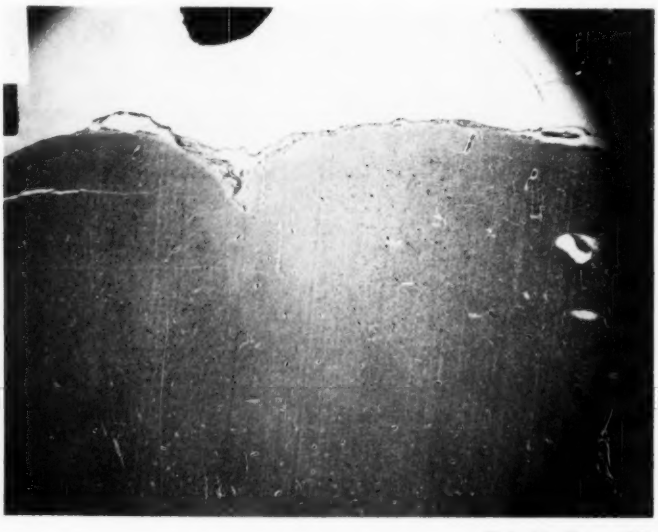


Fig. 3.—Minimal arachnoidal thickening over cerebral convexity three months after application of latex. Weigert's elastic fiber-Van Gieson stain; reduced to 86% of mag. ×25.

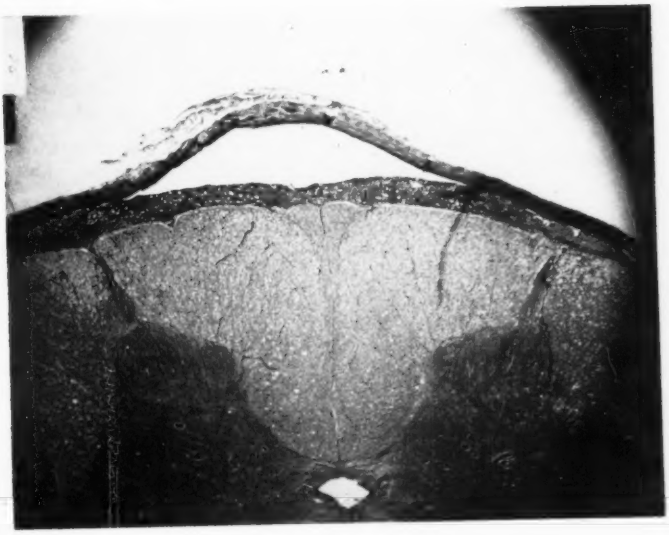


Fig. 4.—Fibrotic layer one month after injection of latex into spinal subarachnoid space. Weigert's elastic fiber-Van Gieson stain; reduced to 86% of mag. × 25.

sponge there is no significant glial reaction or loss of neurons from the cerebral cortex. Beneath a thinner fibrous tissue layer, the dorsal surface of the spinal cord and its coverings show no reaction. Sections of the cord caudal to the experimental lesion do not show degeneration in either the cord or the nerve roots.

Brain wounds covered with latex and gelatin sponge showed fairly extensive meningocerebral cicatrix and appeared different from control wounds in showing a higher concentration of gitter cells at three months.

Physiological Observations.—No paralysis or other loss of function was noted in any of the animals. In one dog with bilateral brain wounds treated with latex, a single seizure occurred five days postoperatively. One dog died one month after the

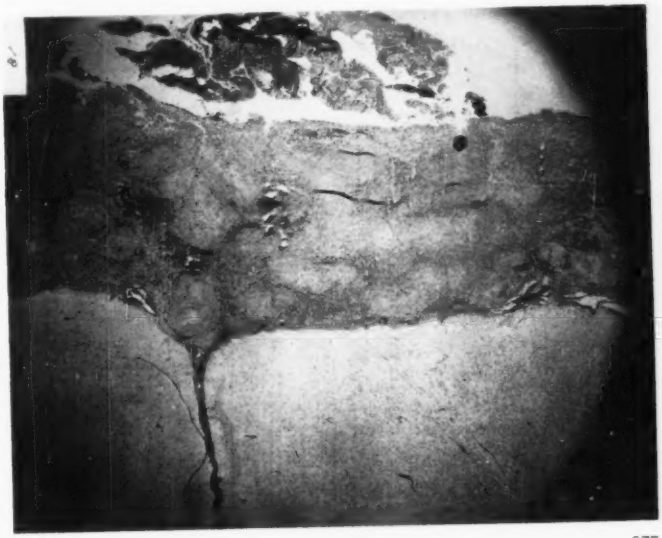


Fig. 5.—Thick fibrotic layer over cerebral convexity one month after application of latex-impregnated absorbable gelatin sponge. Weigert's elastic fiber-Van Gieson stain; reduced to 86% of mag. × 25.

carotid vessels had been coated with latex, but the cause of death could not be determined.

Sterilization Studies.—No bacteria or fungi were cultured from latex sterilized by autoclaving at 240 F for one hour, or from two additional samples subjected to 5.6 mega-rep of gamma radiation. There were no instances of wound infection.

Conclusions

The application of liquid latex to arterial adventitia in the dog produces in two to three weeks a degree of adventitial fibrosis and thickening that would appear to increase the tensile strength of the arterial wall.

Reaction in adjacent tissue is minimal, and sarcogenic properties have not been noted. Sterility of the latex is obtained either from autoclaving at 240 F for one hour or from approximately 5 mega-rep of gamma radiation.

Meningeal and brain reaction is quite minimal with the amount of latex necessary for optimal fibroblastic stimulation. The spinal cord and peripheral nerves with surrounding fibrotic reaction to latex show no change in their own structure.

Latex alone or latex-soaked packs and cuffs of absorbable gelatin sponge and oxidized cellulose will not tamponade acute arterial bleeding. It appears, therefore, that in strengthening arterial walls latex has less value as an alloplastic substance than as an agent for fibroblastic stimulation.

Comment

Pressure measurements in the carotid artery and circle of Willis in man following carotid occlusion have shown that in approximately one-third of cases studied pressure drops of 50% or greater obtain.[2] In such cases the risk of vascular insufficiency and hemisphere infarction is great. The same studies indicate that within certain blind arterial segments created by "trap ligation," residual pressure remains surprisingly high and that aneurysms arising from these segments are therefore incompletely isolated.

Following both intracranial trap ligation and simple cervical ligation, there is a variable, but definite incidence of postoperative mortality and hemiplegia. Less frequently there may be recurrent hemorrhage following cervical ligation. These complications and failures of surgical treatment and the associated technical difficulties of exposure and ligation have been analyzed by various surgeons in separate reports and summarized by Hanbery.[3] The hypothermic state, in addition to giving protection against the effects of temporary lack of circulation, has rendered practicable clear exposure of some aneurysms which otherwise would remain unapproachable. However, the value of hypothermia in preventing later complications of permanent ligation has not been determined. Thus, the hazards related to surgical treatment of intracranial aneurysms result from either attempts or failures to decrease saccular tension from within.

According to Laplace's formulas,[4] "Tension in a dilated wall tends to increase in proportion to radius of curvature of the sacculation." Attempts to reinforce aneurysms with muscle stamps, absorbable gelatin sponge, and oxidized cellulose have many times been unsatisfactory, resulting in recurrent hemorrhage. At the present time liquid latex appears to be the most nearly satisfactory substance for reinforcement of aneurysmal wall. In the repair of human aortic aneurysms, it has been proved a useful agent.[5] Under direct vision it can be applied to the entire surface, and it promotes a uniform, adherent fibrous tissue investment. Adverse tissue reactions are minimal. Whether or not its exclusive use produces reinforcement of sufficient strength to prevent rupture of a dilated wall remains to be determined. As an adjunct to present methods of treating aneurysms, its use would seem to give additional protection.

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Posterior Vaginal Anus*

A Frequently Missed Abnormality

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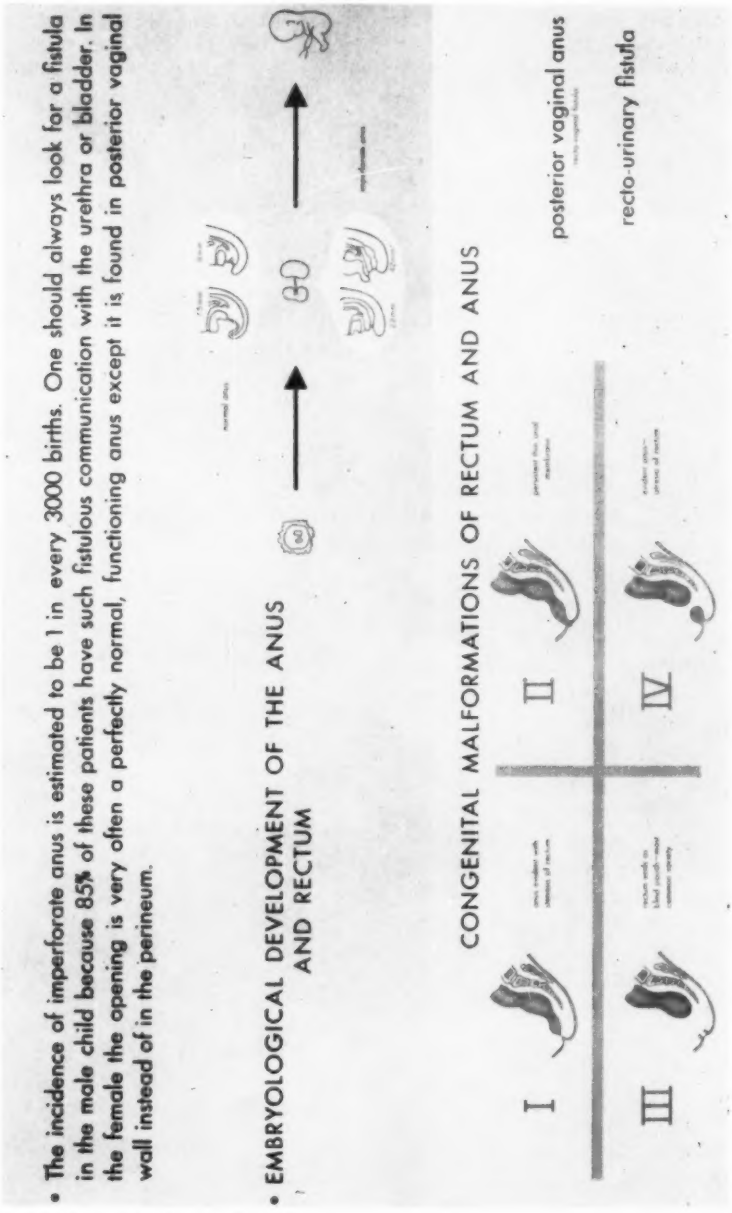
New York


• The incidence of imperforate anus is estimated to be 1 in every 3000 births. One should always look for a fistula in the male child because 85% of these patients have such fistulous communication with the urethra or bladder. In the female the opening is very often a perfectly normal, functioning anus except it is found in posterior vaginal wall instead of in the perineum.
• EMBRYOLOGICAL DEVELOPMENT OF THE ANUS AND RECTUM
CONGENITAL MALFORMATIONS OF RECTUM AND ANUS
I
II
posterior vaginal anus
III
IV
recto-urinary fistula

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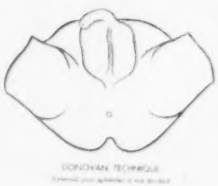
862 Park Ave. (21).

- The male should be operated on within 48 hours after birth, to prevent urinary tract infection.



- The errors in previous surgical management of female infants with type III imperforate anus and posterior vaginal anus, lead us to present the following study.

Male Cases Illustrating Types of Imperforate Anus

Patient	Age	Type Imperforate Anus	Type Fistula	Previous Surgical Management	Corrective Surgical Procedure	Result
W. D.	3 wk.	I	None	None	Dilatation of stenotic rectum	Excellent
Baby T.	24 hr.	II	None	None	Incision of anal membrane and subsequent dilatation	Excellent
M. R.	4 mo.	III	None	None; colostomy performed elsewhere	Abdominoperineal pull-through at age 4 mo.; subsequent closure of colostomy 3 wk. later	Excellent
E. D.	20 hr.	III	Fistula to urethra	None	Abdominoperineal pull-through with division of fistula to urethra	Excellent

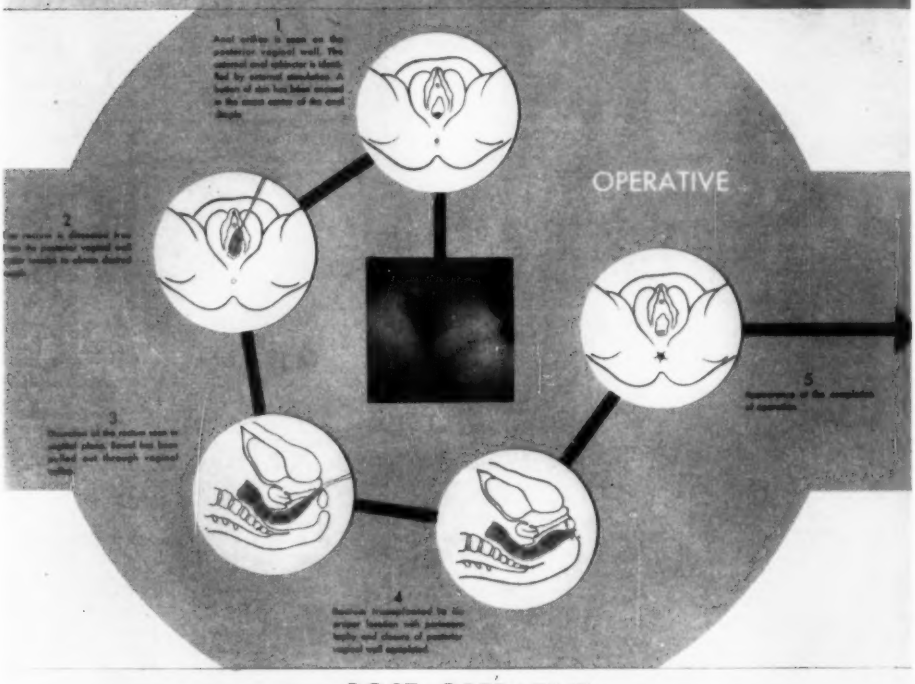
Female Cases Illustrating Previous Surgical Management of Posterior Vaginal Anus and Corrective Surgical Procedure

Patient	Age	Type Imperforate Anus	Type Fistula	Previous Surgical Management	Corrective Surgical Procedure	Result
M. Bu.	2 yr.	III	PVA	Surgery done resulted in a perineal as well as a vaginal fistula, both draining feces	Preliminary colostomy, followed by abdominoperineal pull-through and subsequent closure of colostomy	Fair bowel control
S. F.	1 yr.	III	PVA	Abdominoperineal pull-through at birth (birth weight 4 lb. 9 oz.); subsequent almost complete obstruction at lower rectum	Preliminary colostomy abdominoperineal pull-through and eventual closure of colostomy	Excellent
M. By.	5 yr.	III	PVA	Sigmoid colostomy, which failed to function	Right upper quadrant transverse colostomy; subsequent closure of sigmoid colostomy, followed by 2 abdominoperineal pull-throughs and, finally, closure of transverse colostomy	Good with fair control
C. L.	9 yr.	III	PVA	Several perineal procedures in which coccyx was removed and perineal fistula resulted	Transverse colostomy, closure of perineal fistula, and transplantation of anus to proper location by perineal route and closure of colostomy	Good bowel control
A. D. R.	8 yr.	III	PVA	Delay in surgical correction	Failure of abdominoperineal pull-through because of secondary megacolon; successful result after decompressing colostomy and subsequent pull-through	Good
R. McN.	1 yr.	III	PVA	None	Perineal anoplasty at age 1 yr. with good result; anesthesia and dilatation of rectum necessary at age 4 yr. to remove swallowed metallic foreign body	Excellent

PRE OPERATIVE

Posterior Vaginal Anus

Before surgery, dioctyl sodium sulfosuccinate* in a one percent solution is added daily to the bottled formula in amounts from ten to forty milligrams depending on the infant's weight. If necessary, the posterior vaginal anus is dilated. Neomycin sulfate is administered orally for 48 hours prior to surgery, dosage based on the patient's weight.



POST OPERATIVE

Vitally important post operative dilatation of the new anus is started by the surgeon on the 10th post operative day. A well lubricated nasal speculum or a centrifuge tube is preferable to the gloved finger. The mother must continue this dilatation 2 or 3 times a week. A soft consistency of the stools must be maintained as a fecal impaction must be avoided at all costs.

POSTERIOR VAGINAL ANUS and IMPERFORATE ANUS

general considerations

DIAGNOSIS

- A simple examination of the perineum will reveal the absence of the normal anus. Examination of the vagina will reveal an adequately functioning anus in the posterior vaginal wall.

MANAGEMENT

- In a male or female infant with imperforate anus without a fistula: surgery should be delayed for 48 hours. This allows for recognition of associated congenital defects and enhances the value of X-ray in the inverted position (Wangensteen & Rice).

- Ideally PVA repair in females at 4-5 months and certainly before the menarche.

- Indications for colostomy:
  a. In older children use double barreled colostomy to decompress megacolon before PVA repair.
  b. If the birth weight is 5 lbs. or less, or in an older child—malnutrition.
  c. Where optimum facilities for initial and corrective surgery are unavailable.

- Wetting agents dioctyl sodium sulfosuccinate or mineral oil in older children must be employed pre and post operatively—at all costs avoid impactions.

POST OPERATIVE CARE

- Post operative dilatation of newly constructed anus of importance equal to surgical techniques. This treatment is initiated 10 days post operatively.
- Mother must continue post operative dilatation treatments, possibly as long as one year.
- Parents must persist in toilet training—objective is **regular bowel habits.**

POST OPERATIVE FOLLOW-UP

Group of patients at various post operative intervals. BOWEL CONTROL is more important than appearance of the anus.

baby T 1 year 9 months

A D K 3 months

M R 1 year 6 months

M B Y 1 year 5 months

Gross Autopsy Findings in Cases of Fatal Acute Pancreatitis

IRVING F. ENQUIST, M.D., and MARVIN L. GLIEDMAN, M.D., Brooklyn

Acute pancreatitis is still a very important and unsolved clinical problem. The mortality rate among patients managed even in the best hospitals is disappointingly high. At the present time the consensus indicates that the accepted treatment is nonoperative, operation being reserved only for those patients who develop complications that must be handled by surgical drainage of one form or another.

The symptoms presented by acute pancreatitis are varied; for this reason the diagnosis, often very obvious, can be missed by even the most careful group of clinicians. Unfortunately, also, the study of enzyme derangements in the blood and urine of these patients and the study of x-ray findings are not always specific enough for the clinician to make the diagnosis.

The mechanism of death in this disease is often unknown. Although it has been postulated that a circulating enzyme or enzymes may cause changes in distant organs and tissues, in many cases no known increase in enzyme or enzymes is detectable at the time of death. It has recently been pointed out by Kirby et al.[1] that a rather common cause of death in these patients is delayed hemorrhage in the region of the pancreas and/or from the gastrointestinal tract, but this hemorrhage does not account for many of the deaths from this disease. Because the problem still exists, it was felt that a thorough review of the autopsy findings in a group of patients dying with pancreatitis might show certain clinical and anatomic findings which would lead to a better understanding of the pathologic physiology in this disease.

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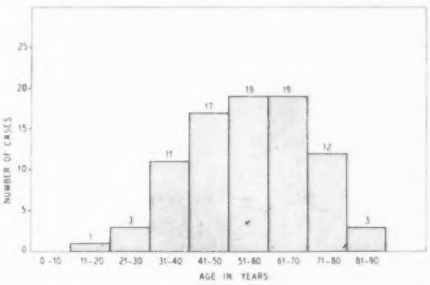
Material

The protocols of all autopsies performed at the Kings County Hospital, Brooklyn, for the years 1939 through 1956 were reviewed, and all patients in whom acute pancreatitis was a major contributing cause of death were studied. Several hundred patients with acute interstitial pancreatitis, in whom this disease did not appear to contribute to death, were excluded from consideration. In the 18-year period of this study 17,289 autopsies were performed; in this group there were 85 cases in which acute pancreatitis was the principal or a major contributing cause of death. This represents an incidence of about 0.5%, a figure close to those of Hamperl,[2] Molander and Bell,[3] and Weiner and Tennant[4]—0.30%, 0.38%, and 0.95%, respectively. A thorough documentation of the specific pathologic findings pertinent to this study was made in each of these 85 cases.

In order to have a control series of patients with which we could compare the frequency of these pathologic findings, the following group of patients was selected: For each patient with pancreatitis, a matched control was selected. Each control case was the patient autopsied nearest in time to the study patient who was of the same age (±5 years), the same sex, and the same color. The patients selected to serve as controls showed no gross or microscopic evidence of pancreatic disease.



Age distribution of 85 autopsied cases of fatal acute pancreatitis.

Findings

Classification.—The cases with pancreatitis were placed in four categories and were found to be distributed as follows:

Acute pancreatic necrosis 14
Acute pancreatic necrosis with hemorrhage 50
Acute pancreatic necrosis with suppuration 12
Acute interstitial pancreatitis 9

The above categories are not meant to represent a complete classification of pancreatitis, but seemed specific and complete enough for our purposes.

Sex.—In the patients dying with pancreatitis, the sex incidence was about equal—44 men and 41 women. However, the sex ratio among the total adult autopsy population in this hospital is 1.6 male to 1 female. This suggests that the disease, at least in fatal form, is commoner in females, if similar percentages of the fatal pancreatitis cases are being autopsied in the two sexes.

Age.—The age distribution is shown in the accompanying Figure. The mean age of the patients with pancreatitis in this series was 55.2 years. The one patient who died of pancreatitis under the age of 21 was a 20-year-old Negro woman who entered the hospital with severe abdominal cramps and vaginal bleeding and was delivered immediately of a stillborn child. Pancreatitis was not suspected, and the patient died. The autopsy revealed very severe, acute hemorrhagic pancreatitis with severe duodenitis, which seemed to cause partial obstruction of the ampulla of Vater.

Postoperative Pancreatitis.—The pancreatitis in 4 of the 85 patients developed immediately after major abdominal operations. The operative procedures performed in these patients were, respectively, cholecystectomy, cholecystectomy with choledochostomy, gastrectomy for gastrocolic fistula, and splenectomy. All of these operations are of types that have been shown by others to be followed by a rather high incidence of postoperative pancreatitis.[5-9] We have on record several other patients at Kings County Hospital who developed what appeared to be fatal acute pancreatitis following gastrectomy, but on whom autopsies were not performed. Acute pancreatitis is not a rare complication following gastrectomy for difficult duodenal ulcer, and the mortality rate is higher in postoperative acute pancreatitis than it is in the idiopathic variety.[6]

Pathologic Findings

Of the many pathologic findings recorded, certain were felt to be more pertinent to the problem of acute pancreatitis than others; they have, therefore, been collected and studied, and comparison has been made of the group of patients with pancreatitis and the group of patients who served as controls.

TABLE 1.—*Pulmonary Pathology in Fatal Acute Pancreatitis*

Pathology	No. of Cases	
	Pancreatitis	Control
Pleural effusion	21	8
Bilateral	14	4
Left	4	2
Right	3	2
Atelectasis	10	2
Bilateral	6	1
Left	3	1
Right	1	0
Pulmonary edema	42	19
Bronchopneumonia	17	19

Thoracic Cavity and Lungs.—In Table 1 is shown the incidence of pulmonary edema and other pathologic pulmonary findings in the two groups of patients. The increased incidence of pleural effusion, pulmonary edema, and atelectasis in the patients with pancreatitis is obvious, and one should note also that the pleural effusion and atelectasis are not confined to the left lung and pleural space. These changes are much more commonly bilateral than unilateral, and occasionally are confined to the right pleural space. In about half of the cases with pancreatitis, the fluid was cloudy and/or sanguineous, and in the other half it was clear and light yellow in color. In the control cases, however, the fluid was clear in all instances and was due to a variety of

TABLE 2.—*Associated Pancreatic Pathology in Fatal Acute Pancreatitis*

Pathology	No. of Cases	
	Pancreatitis	Control
Carcinoma, head of pancreas	3	0
Dilated duct of Wirsung	7	0
Stones in duct of Wirsung	5	0

causes: carcinoma, cardiac failure, etc. The pulmonary edema was bilateral in nearly all cases in both groups. Sanguineous pericarditis with obvious pericardial fat necrosis was found in three of the patients with pancreatitis, but fat necrosis was not seen in any of the pleural cavities. Bronchopneumonia, a common finding at autopsy, was no more frequent in the patients with pancreatitis than it was in the control patients.

Peritoneal Cavity.—Excessive amounts of peritoneal fluid were found in a large number of the patients with pancreatitis. However, only 13 showed serosanguineous or more frankly bloody fluid, and in 10 of these the pancreatitis was of the hemorrhagic type (Table 3); the other 3 died with acute pancreatic necrosis without hemorrhage or suppuration. The fact that none of the patients with interstitial pancreatitis (of sufficient severity to lead to death) had any cloudy or bloody fluid in the peritoneal cavity seems important.

Pancreas.—Pertinent gross pathologic findings in and about the pancreas (exclusive of the inflammation) are shown in Table 2. No report of the incidence of squamous metaplasia in the pancreatic ducts

TABLE 4.—*Gallbladder Pathology in Fatal Acute Pancreatitis*

Pathology	No. of Cases	
	Pancreatitis	Control
Cholecystitis (with stones)		
Chronic	18	18
Acute	3	0
Cholecystitis (without stones)		
Chronic	3	0
Acute	3	0

TABLE 3.—*Abdominal Fluid in Patients with Fatal Acute Pancreatitis* *

Type of Pancreatitis	Total Cases	Clear † Fluid	Cloudy Fluid	Bloody Fluid
Acute interstitial pancreatitis	9	4	0	0
Acute pancreatic necrosis	14	6	1	3
Acute pancreatic necrosis with hemorrhage	30	4	4	10
Acute pancreatic necrosis with suppuration	12	3	3	0

* Fluid, in varying amounts and of all types, was found in 19 of the control cases and was readily explicable in each case.

† All of these, except two in the group with suppuration, were found in cases of cirrhosis, cardiac failure, or metastatic carcinoma.

or of the specific vascular lesions reported by Rich and Duff [10] was made in this series of cases because the organ specimens from the majority of autopsies are not available for resectioning and restudy. Fat necrosis, which was seen in 53 of the 85 patients with pancreatitis, was not found in any of the controls; only 21 of the patients with pancreatitis showed fat necrosis in the peritoneal cavity. All of the lesions listed in Table 2 suggest obstruction in the ductal system, and presumably implicate obstruction in the development of the pancreatitis. Three of the ducts containing stones were dilated. However, none of the three carcinoma cases was associated with dilated ducts. Dilated ducts and ducts containing stones are more frequently associated with chronic pancreatitis than with acute pancreatitis, and in several of these patients

TABLE 5.—*Bile-Duct Pathology in Fatal Acute Pancreatitis*

Pathology	No. of Cases	
	Pancreatitis	Control
Normal common duct with stones	1	0
Dilated common duct with stones	6	2
Dilated common duct without stones	8	1
Perforation, right hepatic duct	1	0
Common channel	9	0
Cancer at ampulla of Vater	1	0
Stone impacted at ampulla of Vater *	6	0
Abnormal fold at ampulla of Vater	1	0

* In two of these cases the bile and pancreatic ducts opened separately.

chronic pancreatitis was described by the pathologists.

Gallbladder and Bile Ducts.—Table 4 shows that the incidence of chronic cholecystitis and cholecystolithiasis in the patients with pancreatitis is not significantly different from the incidence of these diseases in the control patients. However, there is a significant difference in the frequency of acute cholecystitis in the two groups. The frequency of pathologic findings in the common bile duct and in the ampulla of Vater (Table 5) is much higher in the pancreatitis cases than in the control cases and suggests that ampullary obstruction, with or without secondary dilatation of the common bile duct, is related to the genesis of acute pancreatitis. In discussing the importance of biliary tract disease in the origin of pancreatitis, most authors separate cholelithiasis from noncalculous involvement of the biliary tree; the commonly accepted frequency of cholelithiasis in patients with acute pancreatitis is 55%.[11] In the present series the incidence of cholelithiasis in the extrahepatic biliary system was 25% (21 patients) among the control patients and 35% (31 patients) among the patients with pancreatitis. The frequency of the common channel (Table 5) in these patients is probably a minimal figure, because the search for this particular anatomic configuration was made only in those patients with pancreatitis, and certainly not in all of them. A particularly interesting finding in one patient was a perforation of the right hepatic duct; this was not due to an operative procedure. Perforations of the extrahepatic biliary tree in acute pancreatitis have been described by others,[12] and at the present time we have on our service a patient with severe acute hemorrhagic pancreatitis who developed a biliary-cutaneous fistula from the common bile duct.

Liver.—Fatty metamorphosis of the liver was much commoner in the group of patients with pancreatitis than it was in the control group: 32 versus 4. The frequency of cirrhosis, on the other hand, was not significantly different in the two groups: 10 among the pancreatitis cases and 6 among the control cases.

Stomach and Duodenum.—The presence of peptic ulceration and other evidences of acid-peptic disease in the upper gastrointestinal tract was the same in the two groups: six peptic ulcers in each. There were three well-described cases of duodenitis among the patients with pancreatitis and none among the control patients. Gastritis, on the other hand, was found in eight of the patients with pancreatitis and in five of the control patients.

Arteries.—There was a high incidence of moderate to severe atherosclerosis in both groups of patients: 35 in the pancreatitis cases and 32 in the controls. This high incidence in both groups no doubt reflects the age of the necropsy population in this hospital. Deaths from myocardial infarction were about equal in the two groups: two in the pancreatitis cases and four in the controls.

Veins.—Venous thromboses were found in eight of the patients with pancreatitis and in none of the patients in the control group. Six of these eight thromboses were found in major vessels in the region of the pancreas, but because peripheral vessels are not routinely studied at autopsy in this hospital, no information concerning spontaneous peripheral thromboses could be obtained.

Obesity.—The patient was considered obese if the pathologist used the word "obese" in his description of the body before performing the autopsy. No actual weights were determined, but the operating pathologist made and recorded an estimate of the height and weight of each patient before the autopsy was begun. Using the pathologist's description of the patient, it was found that a much greater number of pancreatitis than of control cases was described as obese: 37 as against 9.

Hemorrhage.—Kirby and collaborators[1] pointed out that the pancreatitis patients in their hospital are now dying later during

the disease, and also dying more frequently of delayed hemorrhage than was true of patients studied in their hospital at an earlier period. This exsanguinating hemorrhage occurs into the peritoneal cavity, in the peripancreatic area, or into the gastrointestinal tract. Of the 85 patients with pancreatitis, there was information regarding the exact duration of the disease in only 63. Of these 63, it was found that 40 died within a week of the onset of the disease; 8 died between one and two weeks, and 15 died more than two weeks following the onset of symptoms. There were six patients who died with significant gastrointestinal hemorrhage; in only one of these was the bleeding the likely cause of death, and the duration of the disease in this patient is unknown. In two patients, the time from onset of disease to death is known: three and seven days. In five patients who had severe intraperitoneal and retroperitoneal bleeding without gastrointestinal hemorrhage, the duration of the disease at death was one, three, four, four, and eight days. In only three of these patients was the bleeding severe enough to have been considered the immediate cause of death. Massive gastrointestinal bleeding and/or peripancreatic bleeding, therefore, was not a common final episode in this series of patients with pancreatitis.

Comment

Biliary tract disease with obstruction is thought to play a very important role in the development of many cases of acute pancreatitis. The high incidence of common bile duct stone, dilated common bile duct, and obstruction at the sphincter of Oddi tiates this thesis. The problem of the reflux by tumor and other mechanisms substan- of bile into the pancreas in the etiology of pancreatitis has recently been brought much closer to solution by the work of Elliott and collaborators.[13] These authors showed that, whereas bile alone and bile with pancreatic juice could not be injected into the pancreatic duct under low pressures (and therefore could not cause pancreatitis), bile and pancreatic juice incubated at body temperature for several hours would be readily accepted by the pancreatic ductal system at the same pressure, and this would invariably result in a fatal pancreatitis. This striking demonstration certainly lends support to the common-channel theory for the etiology of pancreatitis.

Our patients with pancreatitis did not have a much higher incidence of cholelithiasis than did the control patients. Apparently, it is not the number of stones in the gallbladder that is important in the causation of pancreatitis, but, rather, it is the number of stones that pass into the common duct and give rise to temporary or persisting obstruction at the ampulla of Vater. Molander and Bell[3] found gallstones six times as frequently in patients with pancreatitis as in the autopsy population at large. Our figures do not show the great difference found by these authors, but the incidence of cholelithiasis in our control patients is about the same as that reported by Ludlow,[14] who studied a large routine autopsy population.

The pulmonary findings in the patients with pancreatitis are striking. Why do these patients develop pulmonary edema? Is it because of circulating trypsin or some other circulating pancreatic enzyme? There is no record in our patients of significant edema in other organs. Perhaps the lung concentrates or elaborates more enzymes than other tissues, or perhaps the pulmonary parenchyma is particularly sensitive to trypsin or other enzyme. The relatively high incidence of pulmonary edema in these patients with pancreatitis should make the clinician particularly wary of this complication.

The high incidence of fatty metamorphosis of the liver in patients with pancreatitis seems significant. Whether the high incidence of obesity in these patients is related to the fatty metamorphosis is unknown. Certainly, sufficient caloric intake alone is not enough to prevent fatty metamorphosis

of the liver, and it is probably true that the fat in these diseased livers is not related to fat deposition elsewhere in the body. Of the 32 patients with moderate to severe fatty metamorphosis of the liver, 14 were obese and 18 were not; 4 of this latter group were markedly emaciated. An accurate alcoholic history had not been obtained in all of these patients so that no figures are available concerning this factor. Lindsay et al.[15] and Popper[16] pointed out the significance of protein deficiency in the etiology of pancreatitis in the experimental animal. Ethionine pancreatitis is felt to be directly related to an interference with protein metabolism in the pancreas, by interfering with the normal metabolism of sulfur-containing amino acids (methionine). It seems, therefore, that fatty degeneration of the liver is not related to caloric intake per se, but that both pancreatitis and fatty degeneration of the liver are related to protein deficiency.

Summary

Eighty-five autopsies on patients with fatal acute pancreatitis were reviewed and compared with the findings in 85 autopsies in a series of matched controls.

1. Pulmonary edema, pleural effusion, and atelectasis were found much more frequently in the patients with pancreatitis than in the control patients.

2. Calculous disease of the gallbladder was found with equal frequency in the two groups, but inflammatory disease of the gallbladder was found more frequently in patients with acute pancreatitis. Inflammatory and calculous diseases in the bile ducts, exclusive of the gallbladder, were found much more frequently in the patients with pancreatitis.

3. Fatty metamorphosis of the liver was found much more frequently in the patients with pancreatitis. Cirrhosis was found with approximately equal frequency in the two groups.

4. The incidence of obesity in the patients with pancreatitis was much higher than the incidence of obesity in the control patients.

5. Severe gastrointestinal and/or peripancreatic bleeding was not a common finding in this series of patients with pancreatitis. However, the patients with pancreatitis in this series died earlier of their disease than was true in a recent series of patients reported in which hemorrhage was a much more frequent complication.

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Results of Major Arterial Grafting*

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Cleveland

Introduction

The symptom of intermittent claudication is due to inadequate blood supply to the claudicating muscles. The symptom of claudication and the physical finding of absence of pulses in the proper location establish a clinical diagnosis of arteriosclerosis obliterans. The location of the occlusion, its anatomic detail, and

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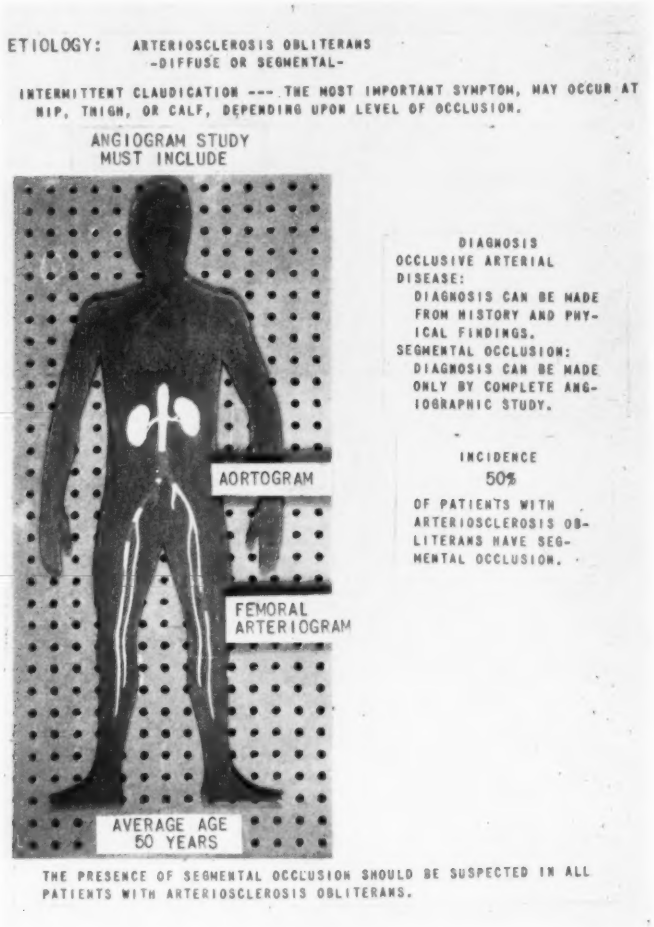
ETIOLOGY: ARTERIOSCLEROSIS OBLITERANS
-DIFFUSE OR SEGMENTAL-
INTERMITTENT CLAUDICATION --- THE MOST IMPORTANT SYMPTOM, MAY OCCUR AT HIP, THIGH, OR CALF, DEPENDING UPON LEVEL OF OCCLUSION.
ANGIOGRAM STUDY MUST INCLUDE
AORTOGRAM
FEMORAL ARTERIOGRAM
AVERAGE AGE 50 YEARS
DIAGNOSIS
OCCLUSIVE ARTERIAL DISEASE:
DIAGNOSIS CAN BE MADE FROM HISTORY AND PHYSICAL FINDINGS.
SEGMENTAL OCCLUSION:
DIAGNOSIS CAN BE MADE ONLY BY COMPLETE ANGIOGRAPHIC STUDY.
INCIDENCE
50%
OF PATIENTS WITH ARTERIOSCLEROSIS OBLITERANS HAVE SEGMENTAL OCCLUSION.
THE PRESENCE OF SEGMENTAL OCCLUSION SHOULD BE SUSPECTED IN ALL PATIENTS WITH ARTERIOSCLEROSIS OBLITERANS.

the collateral pattern are demonstrated by angiology. Approximately 50% of all cases of arteriosclerosis obliterans are amenable to treatment by arterial graft. All abdominal, femoral, and popliteal aneurysms are amenable to treatment by arterial graft.

The results of grafting in 300 consecutive patients are analyzed as to current results and are presented.

In general, it may be stated that between 80% and 85% of patients treated by arterial graft are entirely rehabilitated.

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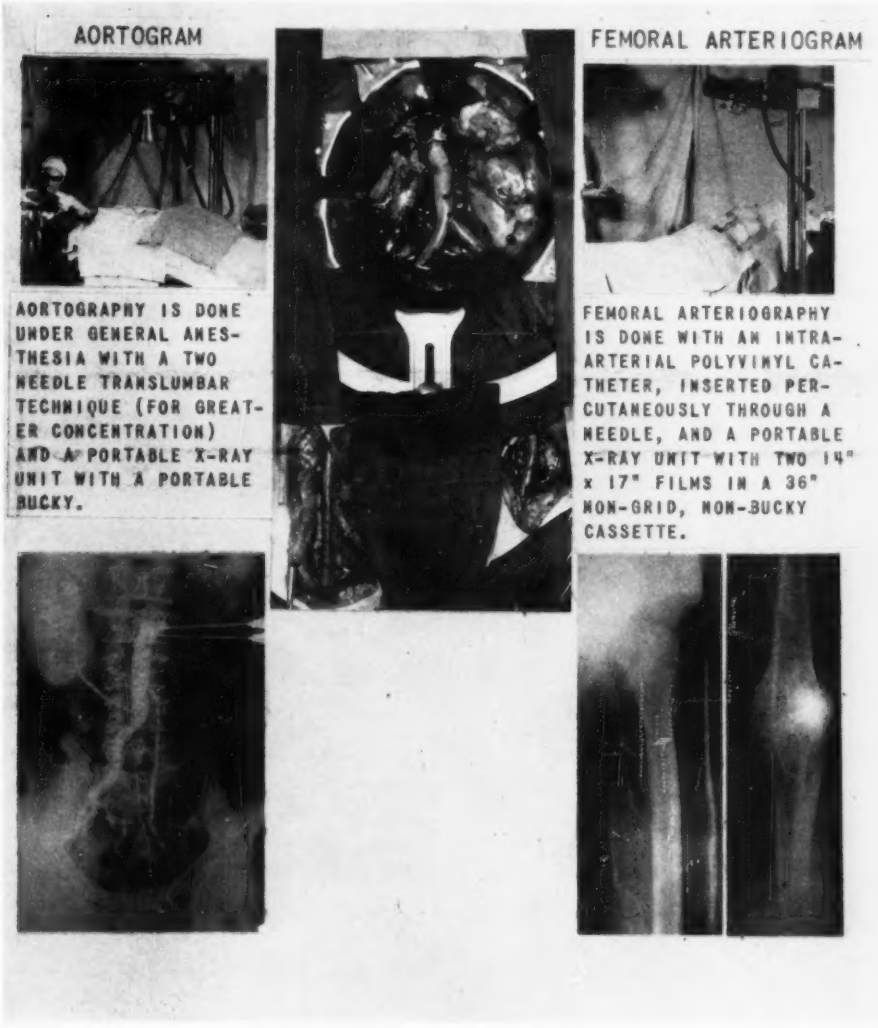
Cleveland Clinic


AORTOGRAM
AORTOGRAPHY IS DONE UNDER GENERAL ANESTHESIA WITH A TWO NEEDLE TRANSLUMBAR TECHNIQUE (FOR GREATER CONCENTRATION) AND A PORTABLE X-RAY UNIT WITH A PORTABLE BUCKY.
FEMORAL ARTERIOGRAM
FEMORAL ARTERIOGRAPHY IS DONE WITH AN INTRA-ARTERIAL POLYVINYL CATHETER, INSERTED PERCUTANEOUSLY THROUGH A NEEDLE, AND A PORTABLE X-RAY UNIT WITH TWO 14" x 17" FILMS IN A 36" NON-GRID, NON-BUCKY CASSETTE.

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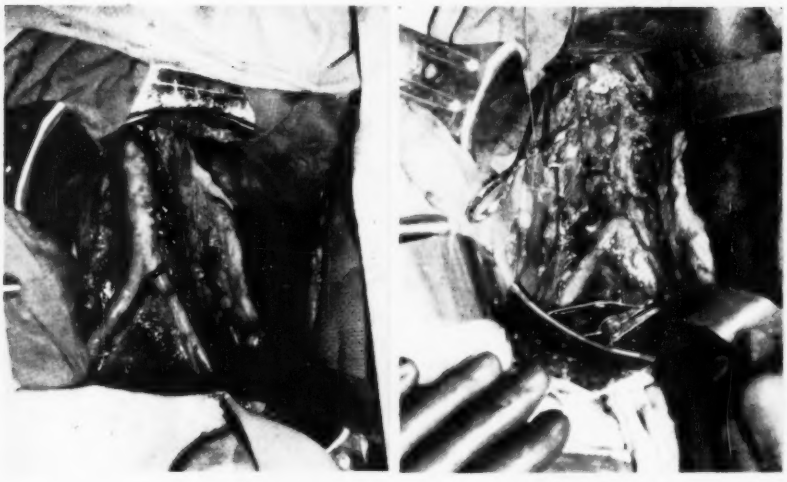

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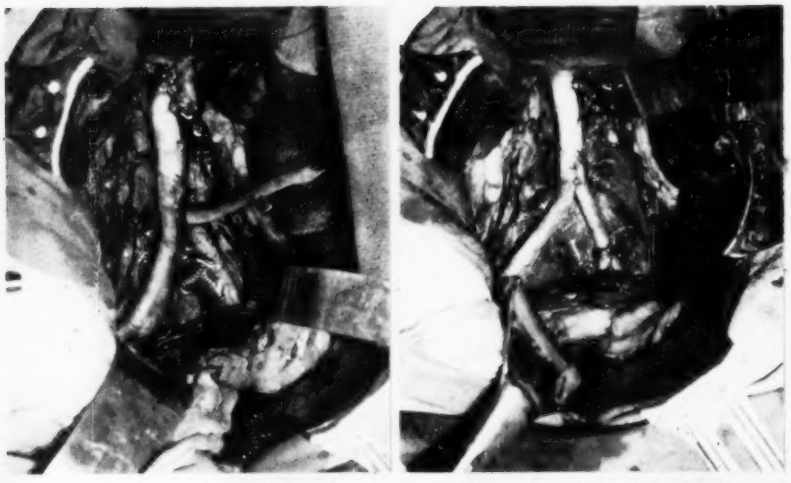
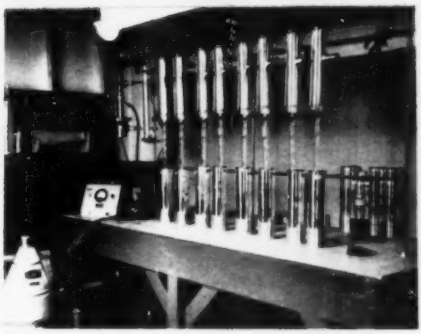
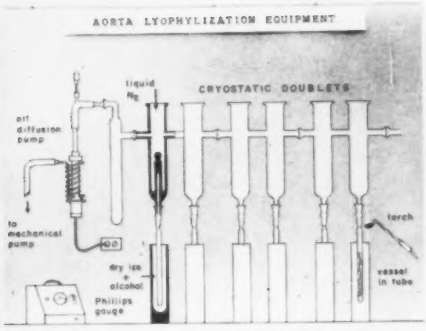


PARTIAL ANASTOMOSIS COMPLETE ANASTOMOSIS

VESSEL BANK





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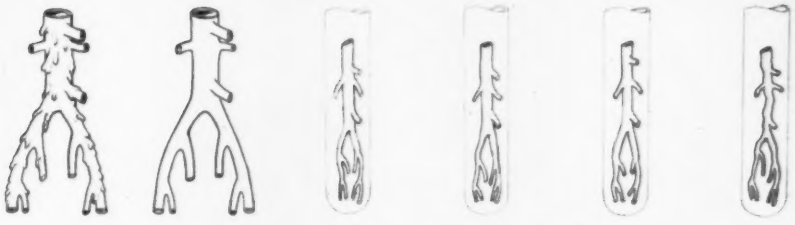

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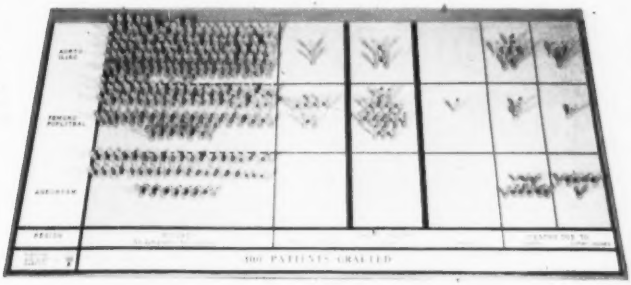

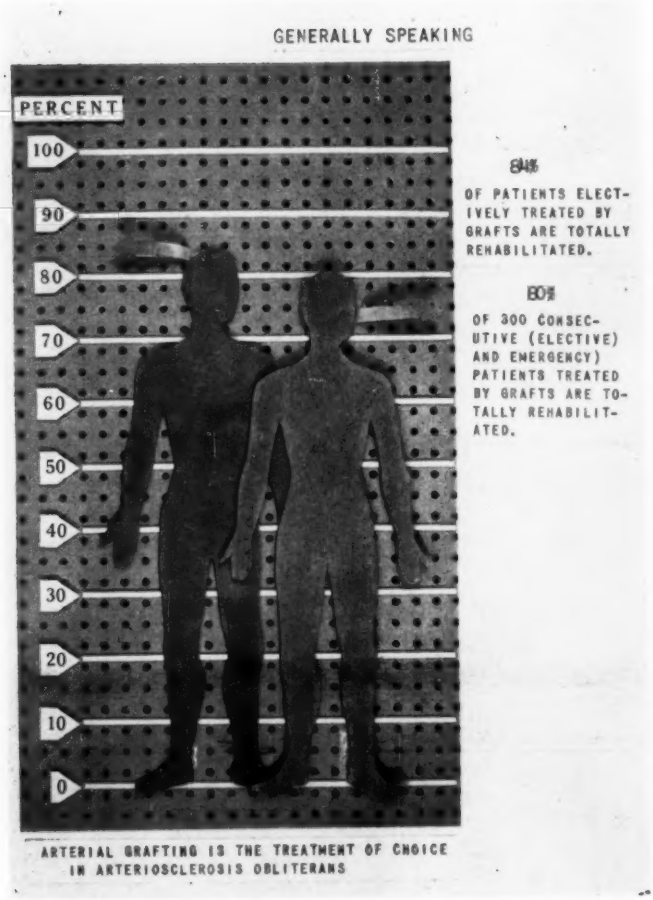
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OF PATIENTS ELECTIVELY TREATED BY GRAFTS ARE TOTALLY REHABILITATED.
OF 300 CONSECUTIVE (ELECTIVE) AND EMERGENCY) PATIENTS TREATED BY GRAFTS ARE TOTALLY REHABILITATED.
ARTERIAL GRAFTING IS THE TREATMENT OF CHOICE IN ARTERIOSCLEROSIS OBLITERANS

Case Reports

Esophageal Hiatus Hernia with Obstructive Incarceration of Pylorus, Pancreas, and Duodenum

THOMAS C. MOORE, M.D., Indianapolis

Symptoms associated with the presence of esophageal hiatus hernia of the diaphragm may vary widely. Often the herniation may produce no symptoms. In other cases the symptoms may be vague ones of indigestion with occasional vomiting. At times, symptoms attributed to the demonstrated presence of an esophageal hiatus hernia may in fact be due to accompanying pathology, such as occlusive coronary artery disease, peptic ulceration of the stomach or duodenum, gallstones, and pancreatitis. Severe episodes of vomiting may be encountered in some cases. Sweet,[5] in 1952, reported the occurrence of obstruction, with intermittent or unrelieved vomiting, in 13 of 111 patients. Incarceration of abdominal viscera with strangulation and gangrene rarely occurs in this type of hernia. The strangulating type of obstruction with gangrene generally is found in the post-traumatic type of diaphragmatic hernia.[1,3]

The major types of esophageal hiatus hernia are the sliding type, in which there is an elevation of the terminal portion of the esophagus with the cardia of the stomach above the diaphragm, and the parahiatal or paraesophageal type, in which the terminal portion of the esophagus is in a normal position with the cardia of the stomach remaining below the diaphragm.[2,5] In the paraesophageal type of hernia the sac generally is occupied by some portion of the fundus of the stomach.

The prolapse of distal stomach, pancreas, and duodenum into the sac through the diaphragmatic defect is rare indeed. I have encountered only one published report of a case of this type. The case was reported by Poppel, Abrams, Handelsman, and Segal[4] in 1954, and involved a 64-year-old woman. The herniation of the pancreas above the diaphragm in this case was suggested prior to operation by the roentgen demonstration of characteristic pancreatic calculi above the diaphragm. Loops of intestine also had been shown to be above the diaphragm. This patient had suffered from frequent episodes of vomiting. At operation the patient was found to have herniation of the distal stomach, pancreas, and duodenum through the defect, in addition to a loop of jejunum and a segment of colon. The herniation in this case was associated with the presence of an enlarging ovarian cyst.

Because of the rare occurrence of this type of esophageal hiatal herniation through the diaphragm, it has seemed desirable to report a case of complete and unrelieved gastrointestinal obstruction due to incarceration of pylorus, pancreas, and duodenum in this type of hernia. The patient was a 67-year-old woman who was severely crippled with rheumatoid arthritis and who suffered from cardiac and hepatic disorders as well. This poor-risk patient was managed successfully by means of a bypassing gastrojejunostomy.

Submitted for publication May 26, 1958.

Aided in part by a grant from the James Whitcomb Riley Memorial Association.

From the Surgical Service, Ball Memorial Hospital, Muncie, Ind., and the Department of Surgery, Indiana University School of Medicine.

Report of Case

The patient, a 67-year-old white woman, was admitted to the hospital on Sept. 7, 1957, because of progressive dehydration, with nausea and vomiting of 10 days' duration. She also suffered from severe, crippling rheumatoid arthritis of 40 years' duration, toxic cirrhosis of the liver, and congestive heart failure. The toxic cirrhosis was presumed to have resulted from the use of gold therapy in an attempt in the past to control her rheumatoid arthritis. She was receiving digitalis for her cardiac disorder. She was unable to retain either liquids or solids by mouth. She also complained of her multiple arthritic deformities, shortness of breath, and intermittent ankle edema. She was unable to walk and moved only with the greatest difficulty.

On physical examination, the patient was found to be an asthenic, dehydrated woman with marked, generalized deformities due to long-standing rheumatoid arthritis. Her right upper extremity was frozen in a fixed position across her lower chest and abdomen. She appeared considerably older than her stated age. Her blood pressure was 100/62. Some rales were heard in both lower lung fields. There was some mild epigastric distention but no epigastric tenderness. More resistance to examination was encountered in both lower quadrants. Her admission hemoglobin was 17.5 gm. %, and her red blood cell count was 5,800,000. The white blood cell count was 6700, with a normal differential count. The blood serology was negative. Except for a trace of albumin, the findings in the urine were essentially within normal limits. The total plasma protein was 6.9 gm., with a reversal of the albumin-globulin ratio. The plasma albumin was 2.4 gm. % and the globulin 4.5 gm. %. The blood cephalin flocculation was 4+ in 24 hours. The total serum bilirubin was 1.0 mg. %. Roentgen study of the chest revealed left-sided cardiac enlargement.

She continued to vomit after her admission to the hospital and appeared unable to retain any of the oral feedings which were attempted on several occasions. Her fluid and electrolyte requirements were met by parenteral means. Her condition failed to improve. Roentgen study of the upper gastrointestinal tract was carried out after the oral administration of iopanoic acid U. S. P. (Telepaque). Rather marked gastric dilatation was observed. The presence of an esophageal hiatus hernia was demonstrated, with apparent herniation of the distal stomach and pylorus through the defect (Fig. 1). No radiopaque medium could be seen to pass beyond the approximate area of the pylorus or proximal duodenum. I first saw the patient in consultation at this time. Despite her wretched general condition, operative intervention was regarded as the only available and effective means of relieving her obstruction, and hence of saving her life.

She was taken to the operating room on Sept. 17. Under general endotracheal anesthesia, the peritoneal cavity was entered through an upper

Fig. 1.—Roentgenogram of the epigastrium following the oral administration of iopanoic acid U. S. P. (Telepaque). The stomach is greatly dilated. The herniation of pylorus and duodenum above the diaphragm is demonstrated.

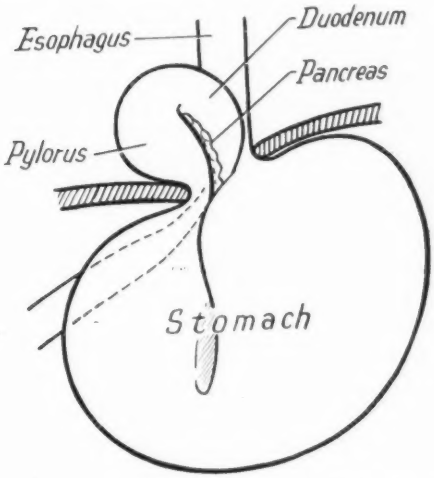

Fig. 2.—Drawing illustrating the herniation of the pylorus, pancreas, and duodenum through a paraesophageal diaphragmatic hiatus hernia defect.

abdominal, midline incision. The stomach was found to be greatly dilated. The cardia of the stomach was inspected and was found to be normal in appearance and position. A right paraesophageal hiatus hernia was found to exist. In the orifice, a loop of pylorus and duodenum, with a small portion of gastric antrum and the head of the pancreas, had become incarcerated and obstructed (Fig. 2). A sliding type of upward herniation appeared to have occurred. However, the herniated structures seemed to be securely fixed in their new position, and they could not be returned to the general peritoneal cavity by traction from below. Although a complete obstruction was observed to exist in this area, there was no impairment of the blood supply to the involved organs. Because of these findings and the very poor general condition of the patient, gastroenterostomy was decided upon as the safest and most direct means of accomplishing the major objective of the operation, the relief of obstruction. Accordingly, an antecolic gastrojejunostomy was created in the area of the most dependent portion of the antrum. A satisfactory lumen was obtained. The incision was closed with interrupted sutures of fine silk. Wire retention sutures also were employed.

The patient tolerated the procedure surprisingly well, considering her poor general condition. Nasogastric suction was maintained for six days following operation. Her postoperative course was essentially uneventful, and her obstruction appeared to have been completely relieved by the bypassing gastrojejunostomy. She was receiving a regular diet and was retaining it satisfactorily at the time of her discharge from the hospital, on Oct. 10. She has continued to do well at home with respect to her gastrointestinal tract.

Comment

Because of this patient's age and wretched general condition, any operative efforts beyond simple relief of the obstruction seemed to be ill-advised. None of the incarcerated structures appeared to be ischemic. However, they could not be returned to the general peritoneal cavity by traction from below. It was clear that a major operative effort would be required to reduce the herniated mass and repair the hernia defect. This did not appear to be justified, and it was feared that the patient would not survive such an effort. The relief of obstruction and the restoration of fluid, electrolyte, and nutritional balance were the principal and most acute objectives, and they were accomplished quite effectively by a simple gastrojejunostomy.

One is tempted to speculate on a possible relationship between the marked deformities of this patient's body and the occurrence of a herniation of the type which occurred here. Certainly, no expanding intra-abdominal mass, as was found in the other recorded case, was present here. The presence of a mass of solid pancreatic tissue in the orifice of the hernia may have been a factor in the production of the type of obstruction observed in this case.

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Rare Primary Somatic Tumors of the Pancreas

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Most primary pancreatic neoplasms, both malignant and benign, are epithelial in nature. Somatic, or nonepithelial, growths from indigenous structures in the pancreas do occur but are extremely rare. The purpose of this article is to report two unusual and rare somatic tumors of the pancreas, both of which were successfully removed. One was a lymphangioma and the other a malignant neurilemoma.

Report of Cases

CASE 1.—*Primary lymphangioma of the pancreas*

A 65-year-old white woman was first seen in June, 1957, with complaints of pain and discomfort in the left upper quadrant of the abdomen. These symptoms were of six months' duration. She was first seen by a private physician, who informed her that she had an enlarged spleen. Another physician, seen in consultation at that time, could not confirm the diagnosis of splenomegaly. She was not given any medication and was told not to worry about it. The patient, however, kept having pain and discomfort in the left upper abdominal quadrant. The pain was intermittent in type, dull aching in character, and not related to respiratory movements. It became progressively worse, especially at night when she turned on her left side while in a lying position. She had no history of fever, jaundice, alteration in bowel habits, or weight loss. Her appetite had been good.

In February, 1957, the patient had x-ray examinations done, which included an intravenous pyelogram, barium enema, and a scout film of the abdomen. These tests showed a normal genitourinary tract, diverticulosis of the colon, and arthritic changes in the lumbar spine. No splenomegaly was detected at that time.

The patient had had known diabetes for the past six years; it had been controlled by diet. She never received any insulin. The patient also had a questionable history of high blood pressure some years before. She had four uneventful pregnancies. Her menstrual history was normal.

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Memorial Center for Cancer and Allied Diseases (Dr. Pack). Doctors Hospital (Drs. Trinidad and Lisa).

Her husband died of cancer of the pancreas. Her mother died of cancer of the stomach, and her brother, of cancer of the liver.

Physical examination revealed a well-developed, well-nourished white woman, who appeared anemic and asthenic. Temperature was 98.6 F; pulse was 72 per minute, and respiration was 16 per minute. Pertinent physical findings were in the abdomen, where a mass was felt in the left upper quadrant. The mass was freely movable and nontender. It was firm in consistency. All laboratory examinations were within the normal range limits.

The patient was operated on in September, 1957. A solid tumor, approximately the size of a large orange, was found presenting itself retroperitoneally and involving the junction of the head and the body of the pancreas. A frozen-section microscopic analysis of the tumor was reported as a possible benign cystadenoma of the pancreas. The mass was then removed by a subtotal pancreatectomy and splenectomy. The tumor was so intimately incorporated in the body of the pancreas as to necessitate the procedure of subtotal pancreatectomy, leaving only a small crescentic remnant of the pancreatic head. The postoperative course was complicated by ileus and the transient appearance of a minor pancreatic fistula. In addition, the patient developed thrombophlebitis and experienced three small episodes of pulmonary embolism. However, she was discharged in excellent condition in October, 1957.

On pathologic examination, the specimen was seen to consist of a thinly encapsulated mass, which measured 6×6×12 cm. The external surface was pink-gray and showed some broad, shallow bosselations. The cut surface (Fig. 1) showed fine, dense fibrous trabeculations. In addition, there were many tiny cysts, some with hemorrhages. The spleen was essentially normal. Histopathologically, the tumor consisted of honeycombed locules, most of which were empty, although some contained clear, acidophilic fluid. These locules were separated by thin, delicate fibrous septa, lined by a single layer of flattened endothelial cells. The septa contained dilated capillaries and aggregates of lymphocytic cells (Fig. 2). The histopathologic diagnosis was lymphangioma of the pancreas.

CASE 2.—*Primary malignant neurilemoma of the pancreas*

A 65-year-old white Peruvian woman was admitted to Doctors Hospital on Dec. 29, 1957, with

Fig. 1 (Case 1).—Primary lymphangioma of the pancreas (hygroma microcysticum). Gross appearance of the tumor at the time of removal. Note the thin external capsule, the trabeculated cut surface, and the small locular spaces.

a history of recurrent upper abdominal pains, of two years' duration. The pains were colicky in nature, occasionally climaxed by emesis. X-ray examination of the gallbladder done in 1955 showed a large, solitary calculus. She gave no history of jaundice or clay-colored stools. There were moderate anorexia and slight loss of weight. Her bowel movements had been regular except for constipation of three days' duration. The pains were recurrent, and two days before admission they became severe and continuous.

She had experienced two previous operations: a nephrectomy for lithiasis, in 1928, and a hysterectomy for fibromyomas, in 1953.

Physical examination revealed a well-developed, acutely ill patient who was having bouts of vomiting and severe upper abdominal pains. Temperature was 100 F; pulse was 80 per minute, and blood

Fig. 2 (Case 1).—Primary lymphangioma of the pancreas. Microscopic appearance of the tumor, showing dilated and cystic spaces lined by a single layer of flattened endothelial cells. Reduced to $\frac{2}{3}$ of mag. $\times 35$.

pressure was 120/80. The heart and lungs were normal. Severe tenderness was elicited over the right upper quadrant of the abdomen, with some muscular rigidity. An ill-defined mass was palpated in the right upper quadrant, which was presumed to be an enlarged gallbladder. The patient also showed an incisional hernia involving the nephrectomy incision. Pelvic and rectal examinations were of no related importance. There were no significant abnormalities in the laboratory examinations.

An emergency laparotomy was performed on Dec. 30. The gallbladder was found to be acutely inflamed and distended. A large calculus was palpated in the lumen of the viscus. The liver was normal to inspection and palpation. A large spherical mass, firm and encapsulated, as well as slightly movable, was palpated in the head of the pancreas. The mass distended the loop of the duodenum. At this time a presumptive diagnosis of carcinoma of the head of the pancreas was made, but no biopsy was done because of the acute inflammation of the gallbladder. The initial operation consisted of a cholecystostomy with removal of the calculus. On Jan. 6, 1958, a second laparotomy was done, at which time a pancreaticoduodenectomy was performed. The distal segment of the pancreas was transected and the duct of Wirsung ligated with silk sutures, after which interlocking silk mattress sutures closed the stump of the residual pancreas without anastomosis. The

Fig. 3 (Case 2).—Primary malignant neurilemoma of the pancreas. Gross appearance of resected specimen. Note the fairly well-circumscribed mass and the periphery showing normal pancreatic tissue.

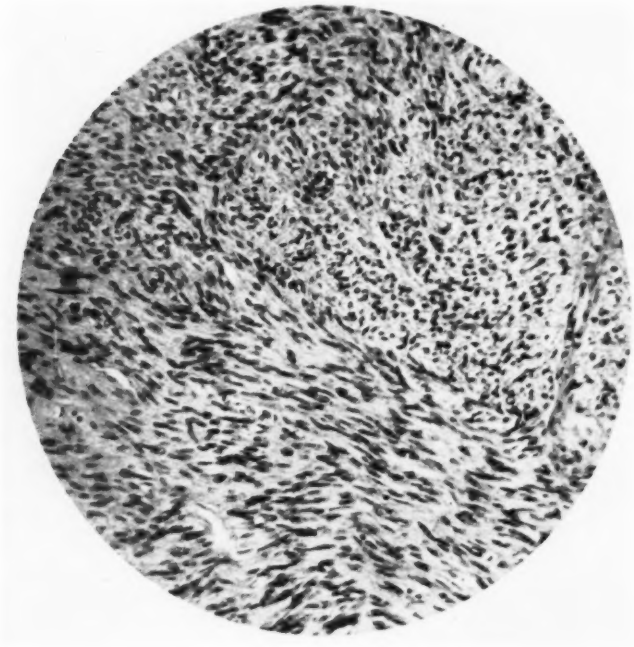

Fig. 4 (Case 2).—Primary malignant neurilemoma of the pancreas. Microscopic appearance of tumor, showing spindle-shaped cells with some palisading. The nuclei are hyperchromatic and show some pleomorphism. Reduced to $\frac{2}{3}$ of mag. $\times 90$.

prepyloric part of the stomach was excised, together with the entire duodenum, the duodenojejunal junction, and the head and a portion of the body of the pancreas. The jejunum was delivered through the transverse mesocolon, and an end-to-end retrocolic anastomosis was constructed between the common bile duct and the jejunal stoma. A distal loop of jejunum was elevated anterior to the transverse colon for a terminolateral gastrojejunostomy.

The postoperative course was complicated by the development of diabetes, which was controlled by diet and insulin. The patient was discharged, in excellent condition, on Jan. 28. She was readmitted two days later because of mild pneumonitis, which soon responded to antibiotic therapy, and she was discharged fully recovered.

Pathological examination revealed the resected specimen to consist of the duodenum with the attached proximal pancreas and portion of the antrum of the stomach (Fig. 3). The head of the pancreas showed a globular mass, which was partially adherent to the serosa of the duodenum. The mass measured 6 cm. in greatest diameter. It was gray-white, lobulated, and streaked with gray and yellow. It appeared encapsulated, and circumferential to the tumor compressed pancreatic tissue was seen. The common bile duct coursed over the tumor and was dilated, but not obstructed. The mucosa was intact and normal. The ampulla of Vater, duodenum, and antrum of the stomach were grossly normal.

Histopathologic examination showed the tumor mass to consist of spindle-shaped cells, arranged in an interlacing pattern. In some regions were cells with tendency to palisading. The nuclei were hyperchromatic and varied in size and shape. Fibrinoid areas of necrosis were encountered, and occasional bundles of nerve tissue were seen. Mitoses were not seen. A Wilder reticulum stain was done and showed the presence of reticulum in long, wiry bundles running between cells. At the periphery of the tumor, normal sections of pancreatic tissue were seen, showing no pathologic changes (Fig. 4). The duodenum, ampulla, and stomach were normal. The histopathologic diagnosis was malignant neurilemoma.

Comment

Visceral hygromas have been rare in our experience. Retroperitoneal cystic lymphangiomas have occurred chiefly in the iliac quadrants in conjunction with more superficial components in the groin, both presumably originating from the primitive lymph cisterns. The pancreatic lymphangioma herein reported was not a retroperitoneal tumor implicating the pancreas by contiguity but originated within the substance of the organ proper, thus necessitating a distal subtotal pancreatectomy.

Malignant neurilemomas may occur anywhere among the somatic tissues, but primary visceral origin is infrequent. In a previous report of 46 cases of malignant neurilemoma by one of us (G. T. P.),[1] a review of the scattergram of distribution does not show a single instance of visceral origin. There has been one benign ganglioneuroma of the stomach wall. Ransom and Kay[2] have reported several cases of these neoplasms of abdominal origin. At the time of operation, the disposition and gross characteristics of the tumor led us to believe the pancreaticoduodenectomy was being done for carcinoma, and the histogenetic diagnosis was not suspected. The prognosis is probably more favorable than for pancreatic cancer; in our previous report there were 59.4% five-year definitive cures for the 46 malignant neurilemomas of general somatic distribution.

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Granuloma Caused by Fishbone in Rectosigmoid Anastomosis

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The anastomosis which is made in the anterior resection for carcinoma of the rectosigmoid must be kept under periodic observation. It is commonly the site of recurrence, and constriction of the lumen, with interference with the free flow of intestinal contents, may occur. The following case is reported to emphasize the fact that narrowing of the anastomosis may entrap a foreign body which may produce a granuloma clinically resembling a recurrence of the carcinoma.

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From the Department of Ano-Rectal Surgery, Mount Zion Hospital and Medical Center.

Fig. 1.—Photomicrograph of primary lesion showing typical changes of adenocarcinoma; low-power lens.

Report of Case

A 61-year-old white man was hospitalized in April, 1952, for a severe myocardial infarction. During his hospitalization rectal bleeding was noted, and sigmoidoscopy was performed. A large, multilobulated tumor of the rectosigmoid (13 cm.) was seen and biopsied; the diagnosis of adenocarcinoma was confirmed by the pathologist (Fig. 1). As soon as the patient was deemed able to undergo radical surgery (May 22, 1952), an anterior resection was performed. There was no gross evidence of metastasis, and no microscopic evidence of spread to the regional lymph nodes. He withstood the procedure fairly well and was discharged 20 days later.

He was reexamined with the sigmoidoscope at six-month intervals, and, except for a moderate constriction at the anastomosis, there were no unusual findings. His bowels moved regularly, and there were no rectal symptoms until November, 1953, when he reported bright red rectal bleeding with bowel movements. Sigmoidoscopy at this time revealed a polypoid lesion on the right lateral aspect of the anastomosis. The greater part of this lesion was removed with the diathermy snare for biopsy, and it was found to contain no neoplastic cells, and was described as granulation tissue (Fig. 2). At this examination the lumen of the anastomosis was seen to have become contracted down to about 1.5 cm. The remainder of the granulation tissue was fulgurated. He was checked in December, 1953, and in March, 1954; his cardiac status precluded any more frequent observation.

In June, 1954, following a second myocardial infarction, he was again hospitalized, and at this

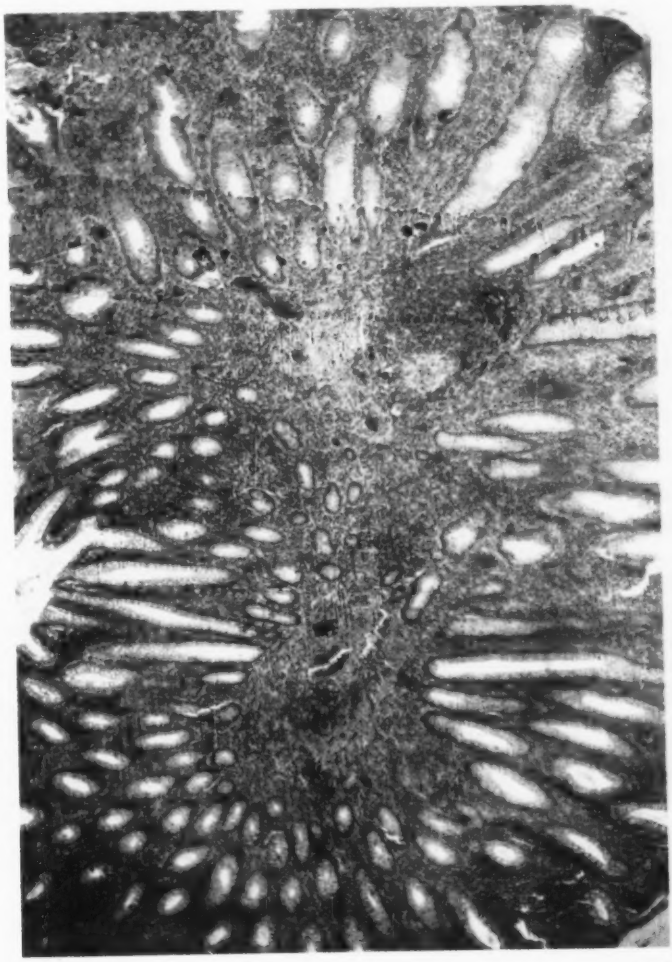

Fig. 2.—Photomicrograph of tissue obtained by biopsy of granuloma, November, 1953, showing one part of the tissue covered by normal rectal mucosa, somewhat distorted by scarring and chronic inflammation in the subepithelial zone. The remainder is granulation tissue infiltrated with lymphocytes, plasma cells, and macrophages.

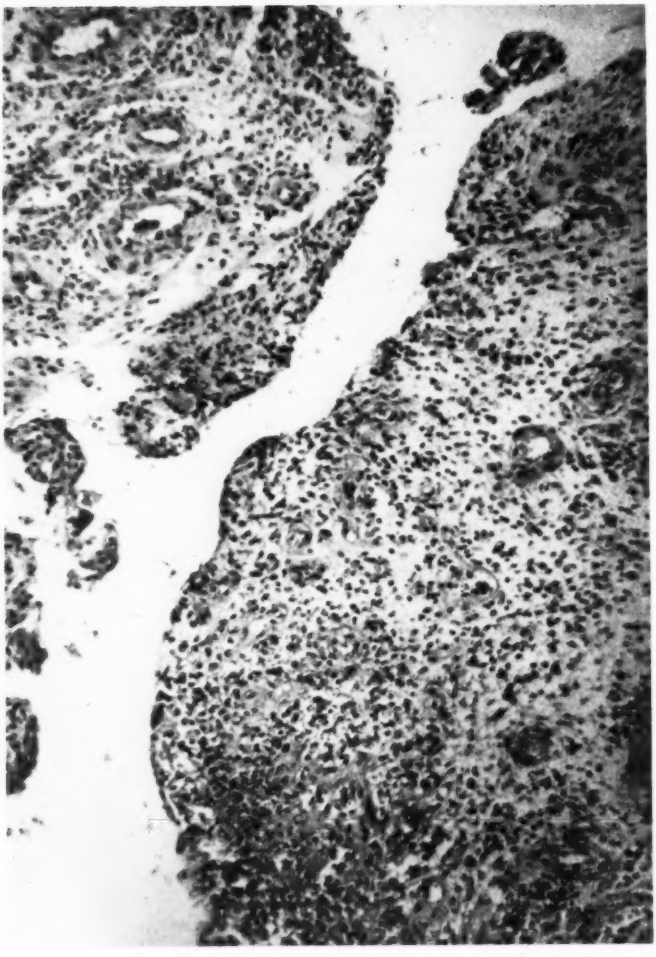

Fig. 3.—Photomicrograph of tissue obtained by biopsy June, 1954, showing tissue composed of rectal mucosa arranged in a modified polypoid form. The glands are fairly deep but lined by normal epithelial cells. There is an outstanding infiltration of lymphocytes, plasma cells, and eosinophils, and these extend into the muscularis mucosa.

time, sigmoidoscopic examination revealed a recurrent granular polypoid mass, deeper in color and smaller in size, than the one previously visualized. Biopsy of the lesion revealed an intense chronic inflammatory reaction, the inflammatory characteristics being much more marked than before (Fig. 3). At a follow-up examination two weeks later, a dark, pointed object was seen projecting upward from the right lateral aspect of the anastomosis. This was manipulated and grasped with the alligator forceps, and proved to be a bone, about 2 cm. in length (Fig. 4).

He has been examined every three or four months since then. No further granulation tissue has appeared. The anastomosis has scarred down smoothly to a diameter of 1 cm., but this is adequate for regular bowel function. He was last seen in April, 1958, approximately six years after the anterior resection.

The unusual features of this case were the appearance of a foreign-body granuloma at the anastomosis 18 to 24 months postoperatively. The cause of the granuloma was a sharp, pointed fishbone which was impacted in the anastomosis. It seems unusual that no perianastomotic abscess or fistula formed, and that there were no other local signs of inflammation.

Fig. 4.—Photograph of fishbone removed from the anastomosis in June, 1954.

Summary

A foreign-body granuloma caused by a fishbone impacted in an anastomosis of the rectosigmoid clinically resembled a local recurrence. Removal of the bone resulted in early resolution of the inflammatory reaction.

Emphasis on the stenosis occurring at the site of the anastomosis as a clinical feature of scar formation is made. Such stenosis is conducive to the entrapment of foreign bodies.

Periodic reexaminations are essential.

A six-year follow-up is presented.

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Congenital Atresia of the Sigmoid Colon

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Congenital atresia of the sigmoid colon is a rare anomaly. Its reported incidence varies considerably.[3,5,6,8,9,11] A more accurate estimate of its infrequency may be gained from the fact that only four recorded cases of survival after surgical treatment were found. The embryology, pathology, clinical features, and treatment of intestinal atresia have been adequately reviewed by others.[3,6-11] Our purpose is to describe a patient with complete atresia of the sigmoid colon who recovered satisfactorily after surgical management.

Report of Case

A white male infant was born at 4:45 a. m. on Jan. 29, 1957. Weight at birth was 5 lb. 3 oz. (2353 gm.). The mother's gestation was full term. Labor and delivery were uncomplicated. After birth, no meconium stool was passed, and at 26 hours of age vomiting of a small amount of greenish-tinged mucus occurred. Attempts at feeding during the next few hours were followed by vomiting of bile-stained material.

Physical examination disclosed moderate abdominal distention. Digital rectal examination revealed an empty rectum with a narrow lumen, but no obstruction was encountered. An enema, consisting of 1½ oz. (45 cc.) of water was administered, which was followed by the expulsion of a small mucous plug from the rectum. Laboratory examinations of the blood and urine were within normal limits. Roentgenograms taken when the patient was 36 hours of age showed distention and fluid levels in the small intestine. Distention of the colon with irregular mottling throughout its entire course was also observed (Figure). Films were obtained in both the upright and the inverted position. A barium enema was considered unsuccessful because the barium ascended only to the lower sigmoid, where an obstruction was encountered, and the contrast material was rapidly expelled during the examination. The point of obstruction corresponded to the area on the abdominal film marking the termination of the distended colon. Atresia of the sigmoid colon was, therefore, considered the probable cause of the obstruction, and surgical intervention was decided upon.

Congenital atresia of the sigmoid colon.
Upright abdominal film showing dilated end of sigmoid colon at point of atresia.

Preoperatively, Wangensteen suction through a nasogastric tube was instituted and a venotomy performed, placing a polyethylene tube in the right saphenous vein at the ankle. The administration of fluids, through the "cut down," was begun, and preparations for operation were made.

Operation.—The operation was performed when the patient was 56 hours of age. A paramedian incision in the left lower abdominal quadrant was used. When the peritoneal cavity was opened, moderate distention of the entire small intestine and large intestine to the midsigmoid was seen. In this area the dilated portion of the colon, which was about 5 cm. in diameter, ended abruptly, and distally the colon was about 2 cm. in diameter. No loss of continuity was present. The atresia was approximately 15 cm. from the anal orifice. The

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From the Department of Surgery, St. Anne's Hospital.

pelvic colon was mobilized by cutting along the lateral peritoneal reflection. The segment distal to the atresia was injected with isotonic saline solution through a small hypodermic needle. The saline solution readily ran out through the anus; so it was obvious that no other area of atresia existed. The distal segment was then brought along the side of the dilated proximal loop, and a side-to-side anastomosis was made between the two intestinal loops which circumvented the area of atresia. During this phase of the operation it was possible to demonstrate a complete septum across the lumen of the bowel, causing the atresia. The anastomosis was done, using an interrupted 0000 silk suture for the seromuscular layer and an interrupted 00000 chromic intestinal absorbable surgical (gut) suture for the mucosal layer. The internal diameter of the anastomosis was about 3.5 cm. When the anastomosis was completed, a catheter passed upward through the anus easily went through the anastomosis, constituting a second demonstration of the patency of the intestinal canal below the area of atresia. The catheter was withdrawn, and the abdominal incision was closed, using fine chromic absorbable surgical suture for the peritoneum, an interrupted 0000 silk suture for the fascia, and an interrupted silk suture for the skin.

Postoperatively, the course was satisfactory. A meconium stool was passed the day after operation. Intragastric suction was discontinued on the third postoperative day and oral feedings started. Oxygen was administered for the first 24 hours postoperatively. A penicillin-dihydrostreptomycin preparation (Combiotic) and ascorbic acid were given for the first week after the operation. Parenteral fluids were not used after the third postoperative day.

On several occasions a small amount of blood was noted in the stool, but this ceased and the baby was discharged on the 20th postoperative day, weighing 6 lb. 2 oz. (2778 gm.).

Subsequent examinations show normal growth and development, with no symptoms referable to the corrected defect. A barium enema taken at 10 months of age revealed no abnormalities in the colon.

Comment

Recently, Chester and Robinson[2] reviewed all the cases of atresia of the colon surviving after surgical intervention. There was a total of 11 patients, including the 4 with atresia of the sigmoid listed in the accompanying Table. Because so few patients have recovered after correction of this defect, it is difficult to evaluate any specific operative procedure used. Various operations were performed in the successful cases. Side-to-side anastomosis, as used in our patient, was followed by a good result in one other patient with sigmoid atresia[3] and in three patients with atresias in other areas of the colon. Until more cases are reported, the ideal method may not be determined. It is possible that side-to-side anastomosis around an area of intestinal atresia is not the best operation to select. The objections to this procedure include postoperative dilatation near the stoma, with blind-loop formation and ulceration with resulting anemia. These undesirable effects have been emphasized by a number of authors, including Clawson,[1] who reviewed previous publications and presented a case of his own. Nevertheless, many patients with intestinal lesions treated by side-to-side anastomosis have survived without developing any untoward sequelae. Perhaps exteriorization of an atretic site in the colon

Reported Cases of Atresia of the Sigmoid Colon Surviving Surgical Correction

Author and Year		Age	Sex		Treatment	Result
Gaub 1922		33 hr.	M		Colostomy	Satisfactory (3-yr. follow-up)
Gann and Hoffman 1952		62 hr.	?		Two-layer, side-to-side anastomosis	Satisfactory
Feggetter 1953	(1)	3 days	M	(1)	Transverse colostomy	Satisfactory
	(2)	36 days		(2)	Lateral anastomosis	
	(3)	48 days		(3)	Relief of acute intestinal obstruction due to adhesions of small intestine with colostomy	
	(4)	55 days		(4)	Resection of fecal fistula and anastomosis	
	(5)	2 mo. later		(5)	Closure of colostomy	
Gerrish 1955	(1)	1 day	F	(1)	Resection of atresia with end-to-end anastomosis and tube cecostomy	Satisfactory (4-yr. follow-up)
	(2)	19 days		(2)	Tube cecostomy (1st cecostomy tube inadvertently removed)	

with subsequent irrigations to dilate the distal narrowed bowel followed by later resection and primary end-to-end anastomosis might be the operation of choice. However, there is a strong desire on the surgeon's part to correct a congenital anomaly at one operation if it is reasonably possible.

It is certain that no disagreement exists concerning the value of early diagnosis, correction of fluid and electrolyte imbalance, decompression of the intestinal tract, good anesthesia, and early operative intervention in the treatment of intestinal atresia. The operation must include exploration for other intra-abdominal anomalies.

Postoperatively, the administration of oxygen, antibiotics, and adequate fluids is important.

Summary

An infant with complete atresia of the sigmoid colon recovered satisfactorily after primary side-to-side anastomosis was done to circumvent the atretic area.

We believe this to be the fifth reported case of successful surgical management of atresia of the sigmoid colon.

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Acute Appendicitis Following Retention of Barium in the Appendix

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Little attention has been given to the significance and possible sequelae of retention of barium in the appendix following a barium meal or enema. Failure of the appendix to fill in the course of either examination is not considered to be of significance. If barium is demonstrated, some positive information is gained in regard to the location. Occasionally, nonopaque fecaliths or kinks in the lumen may be seen. It is usually stated in radiological monographs that the appendix empties itself simultaneously with the cecum or within 24 to 48 hours. When an apparently normal appendix fills with barium, repeat x-ray studies are rarely recommended to determine whether the appendix has evacuated the barium.

Barium is not irritating to the lining of the gastrointestinal tract. However, when retained in the appendix, it may form the nidus of a fecalith, which the appendix may be unable to extrude. Its retention might be indicative of some narrowing of the lumen, such as is caused by kinking, peritoneal bands, or lymphoid hyperplasia. Once present, a fecalith may obstruct the lumen and initiate an acute inflammatory reaction in the appendix distal to the point of obstruction.

Experience with three patients who developed acute appendicitis following retention of barium in the appendix has led to a review of the problem. Brief summaries of the three cases are presented.

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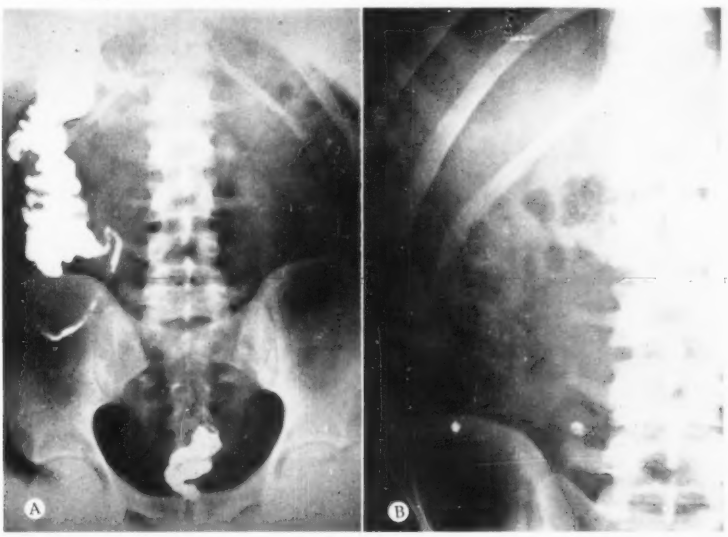
From the Department of Surgery, the Riverside Clinic.

Fig. 1.—*A*, filling of appendix noted on evacuation film after barium enema. *B*, retention of barium in appendix nine days after barium enema.



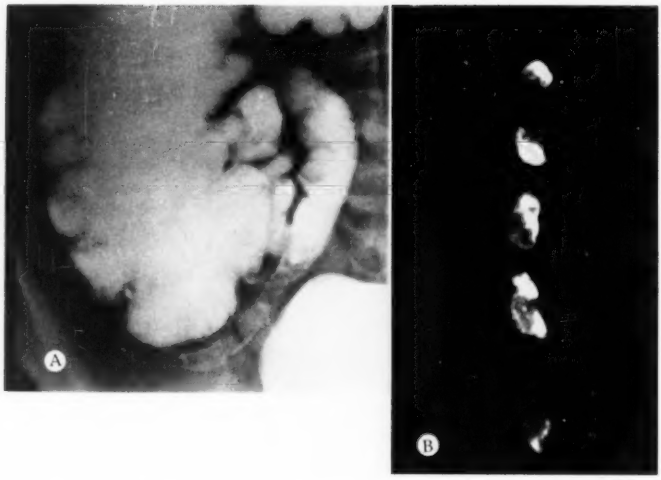


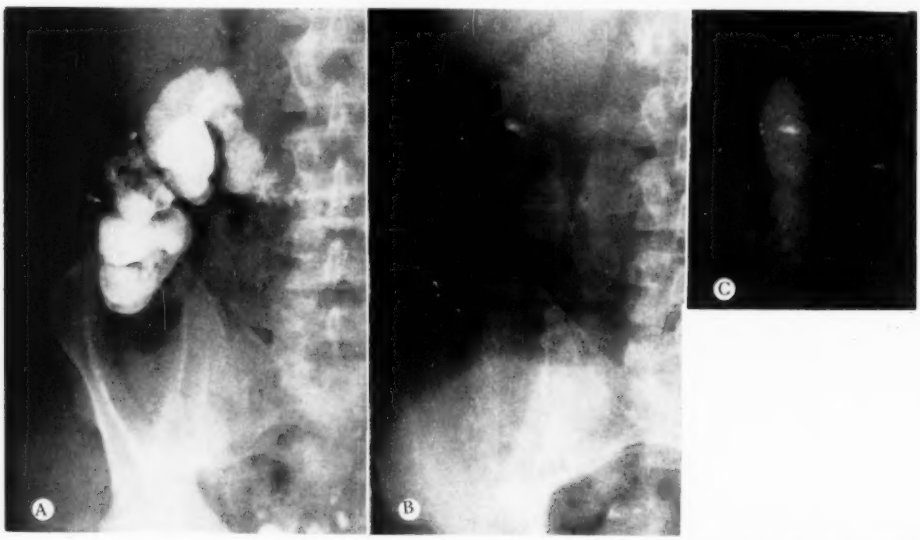
Fig. 2.—*A*, partial filling of appendix noted on barium study. *B*, x-ray of fecaliths from the acutely inflamed appendix removed nine days after administration of barium.

Report of Cases

CASE 1.—The patient was a 20-year-old youth. A barium enema was performed in the course of studying a vague, recurring abdominal pain. The examination was reported negative; the appendix was demonstrated (Fig. 1*A*). Nine days later, retention of barium in the appendix was noted on a cholecystogram (Fig. 1*B*). On the following day, the patient noted the onset of right lower abdominal pain, and 18 hours later, a clinical diagnosis of acute appendicitis was confirmed at operation and the appendix removed. An obstructing fecalith was present in the specimen, which was not x-rayed. Recovery was uneventful.

CASE 2.—The patient was a 19-year-old youth. The appendix was demonstrated in the course of a barium meal study performed to investigate symptoms suggestive of a possible duodenal ulcer (Fig. 2*A*). Nine days later, an acutely inflamed appendix was removed after a 12-hour history typical of appendicitis. An x-ray of the numerous fecaliths removed from the specimen demonstrated

Fig. 3.—*A*, marker indicating barium in distal end of high-lying retrocecal appendix. *B*, marker indicating retained barium in appendix 48 hours after barium enema. *C*, x-ray of specimen showing barium nidus in obstructing fecalith.



the retained barium (Fig. 2*B*). Recovery was uneventful.

CASE 3.—The patient was a 48-year-old man. A barium enema was performed to investigate recurring attacks of mild left lower abdominal pain. Diverticulosis of the sigmoid colon was demonstrated and filling of a high-lying, retrocecal appendix noted (Fig. 3*A*). A film of the abdomen obtained two days later revealed a small amount of barium still present in the region of the appendix (Fig. 3*B*). Fifteen weeks later, the patient developed severe pain in the right abdomen, accompanied by nausea and vomiting. An acutely inflamed, perforated retrocecal appendix was removed 28 hours after onset of symptoms. The specimen contained an obstructing fecalith, the nidus of which was composed of barium (Fig. 3*C*). Recovery was uneventful.

Comment

Although there may be several different causes of acute appendicitis, an obstructing fecalith is generally conceded to be the commonest etiologic factor. Bowers'[1] study has emphasized the increasing frequency with which fecaliths are found in the more complicated forms of appendicitis (Table). The obstructive type of appendicitis is more apt to proceed to perforation and the ensuing complications.

It has been estimated that 10% to 15% of appendiceal fecaliths are opaque to x-rays.[2] Since an x-ray of the abdomen is usually not obtained in the ordinary case of appendicitis, preoperative recognition of opaque fecaliths is uncommon. In a survey of the literature, Felson and Bernhard[3] noted that perforation occurred in 47 of the 99 recorded cases of appendiceal calculi in which this complication was mentioned. Perforation occurred in four of their eight patients with appendiceal calculi having symptoms and treated surgically. In three cases observed personally, the appendiceal calculi, which had been diagnosed by preoperative x-rays, were found free in abscess cavities. Felson and Bernhard[3] concluded that the presence of stones in the appendix is an indication for immediate operation, whether or not the patient has symptoms referable to the appendix. The possibility should be entertained that the same consideration be given in instances in which barium is permanently retained in the appendix.

Incidence of Fecaliths in Various Groups of Appendices *

	Per Cent
Appendicitis with localized peritonitis	90
Appendicitis with generalized peritonitis	86
Appendicitis with gangrene	65
Appendicitis, acute	38
Interval appendectomy	29
Incidental appendectomy	25

* From Bowers.[1]

The paucity of reports of acute appendicitis developing in appendices retaining barium may be only an indication of the infrequency of its recognition. Inquiry regarding previous barium examinations is seldom made in obtaining the history of patients with suspected appendicitis. Abdominal x-rays are not indicated in the usual case of appendicitis, and x-rays of the operative specimens containing fecaliths are rarely made. Increased awareness of the possibility that retention of barium in the appendix may predispose to acute inflammation will lead to recognition of more cases.

In the cases reported herein, retention of barium in the appendix was noted coincidentally on a subsequent cholecystogram in Case 1. Acute appendicitis developed 10 days after administration of the barium. In Case 2, knowledge that the appendix had recently filled with barium led to an x-ray of the acutely inflamed appendix removed nine days after administration of the barium. In Case 3, the patient developed acute appendicitis 15 weeks after retention of barium in the appendix. Perforation occurred prior to operation. Fortunately, his convalescence was uneventful.

Gubler and Kukral[4] reported four cases in which acute appendicitis developed after retention of barium in the appendix from six weeks to several years. Perforation occurred in three of their four cases, with one fatality. They recommended repeat x-ray examinations in every patient whose ap-

pendix filled with barium and interval appendectomy if the barium was still present after one month.

At the present, there is insufficient available information to allow definite conclusions to be reached as to the period that should elapse before recommending elective appendectomy. It is established that prolonged retention of barium in the appendix can lead to acute obstructive appendicitis. I am in agreement with Gubler and Kukral [4] that elective appendectomy should be recommended. However, it is believed that further studies are in order to ascertain the incidence of retention of barium in the appendix following x-ray studies, how long it may be retained before being spontaneously extruded, and, if possible, to determine the incidence of the development of acute appendicitis in those instances in which barium is permanently retained.

In two of the three cases described herein, the inflammatory process developed in less than two weeks after retention of the barium in the appendix. Elective removal of the appendix in less than two weeks can not be recommended on the basis of this very limited experience. It would seem wise to advise such a patient that the presence of the barium in the appendix possibly signifies an abnormal state of that organ and that an increased chance of developing appendicitis exists. Such persons should be advised to report promptly for examination if any of the symptoms are noted at a later date. It is hoped that after further study of the problem, it will be possible to arrive at more definite conclusions regarding the time interval after which elective appendectomy should be recommended for chronic retention of barium in the appendix.

Summary

Barium retained in the appendix may form the nidus for a fecalith, which, in turn, may lead to obstructive appendicitis and its complications. Three cases are reported in which this sequence of events was recognized.

A patient whose appendix retains barium longer than one week after an examination should be advised of the possibility of an abnormal state of that organ and an increased chance for subsequently developing appendicitis. Elective appendectomy should be considered in those instances in which barium is retained longer than one month.

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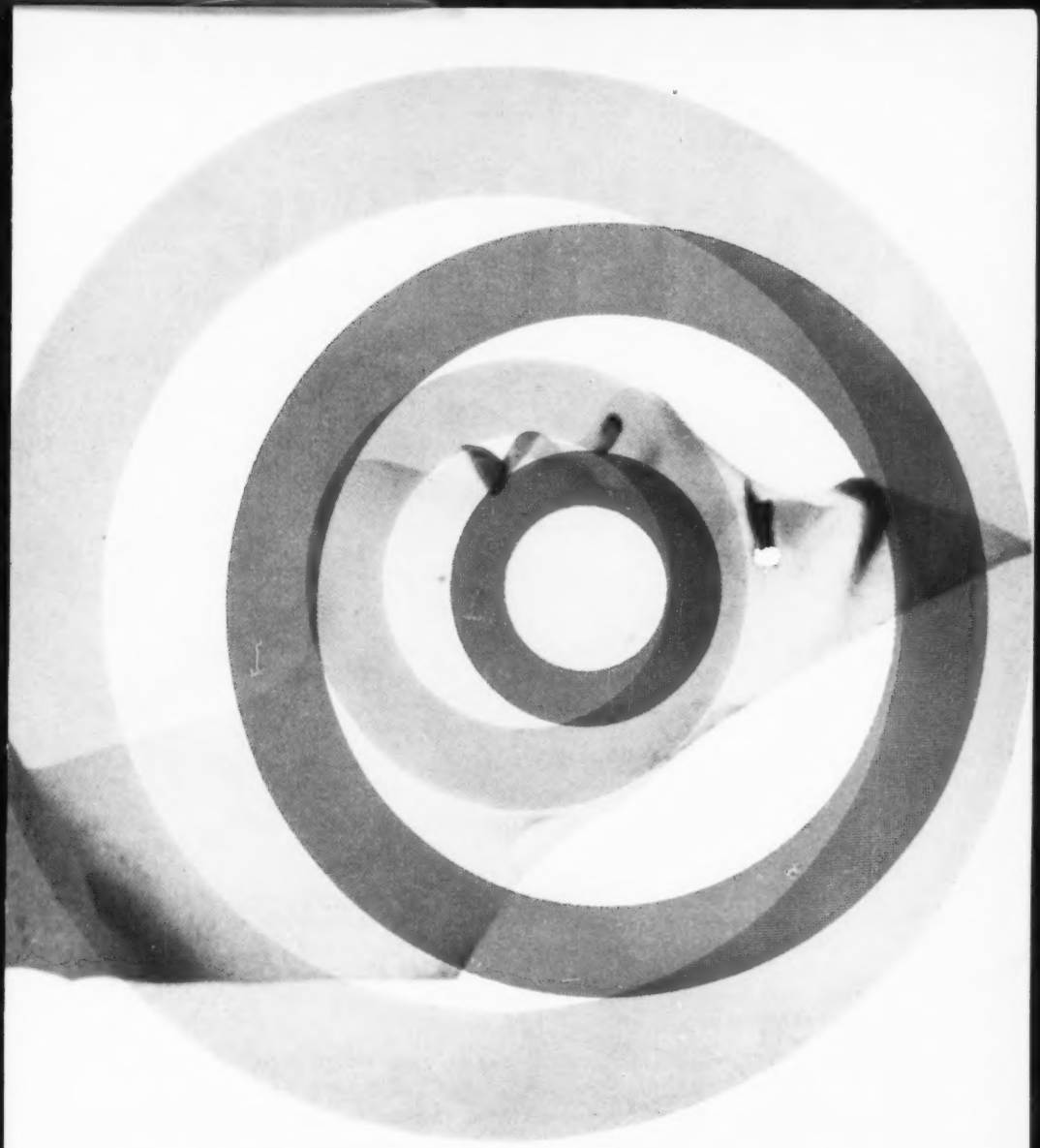

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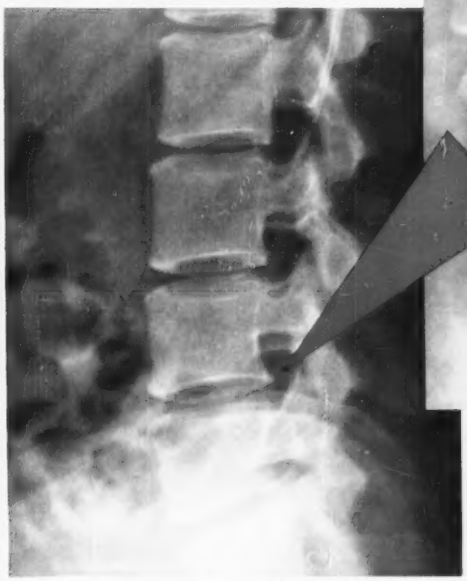
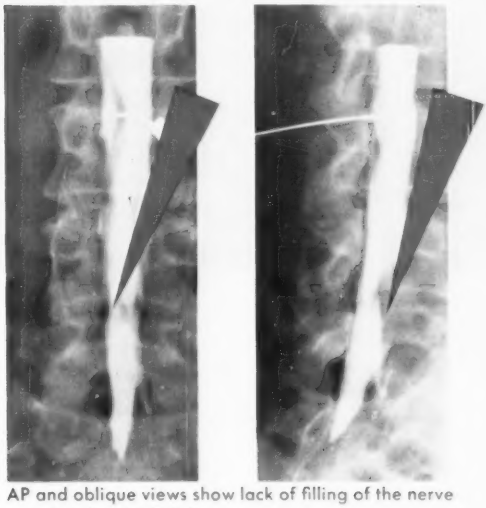


Routine lateral radiograph shows loss of normal lumbar lordosis, also spur formation.

Lateral radiograph (patient supine) with opaque oil in subarachnoid area shows anterior filling defect at the L4-5 disk space.



AP and oblique views show lack of filling of the nerve root sheath at L4-5 disk space.

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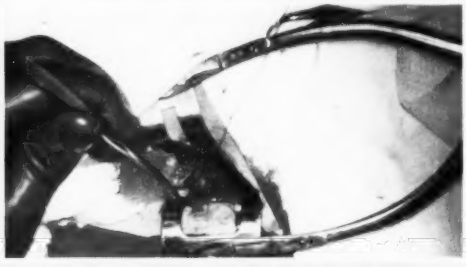
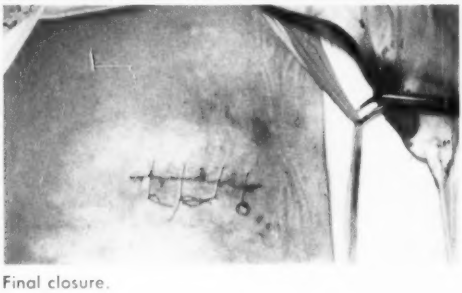


Dura retracted, exposing flattened nerve root.

Nerve root retracted; disk sequestrum extrudes spontaneously.

Disk sequestrum being withdrawn.



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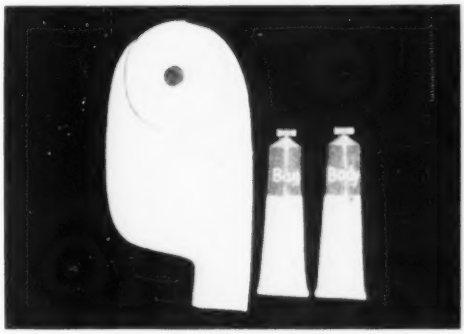

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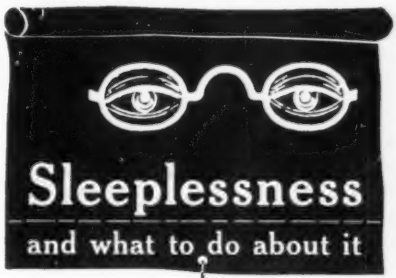

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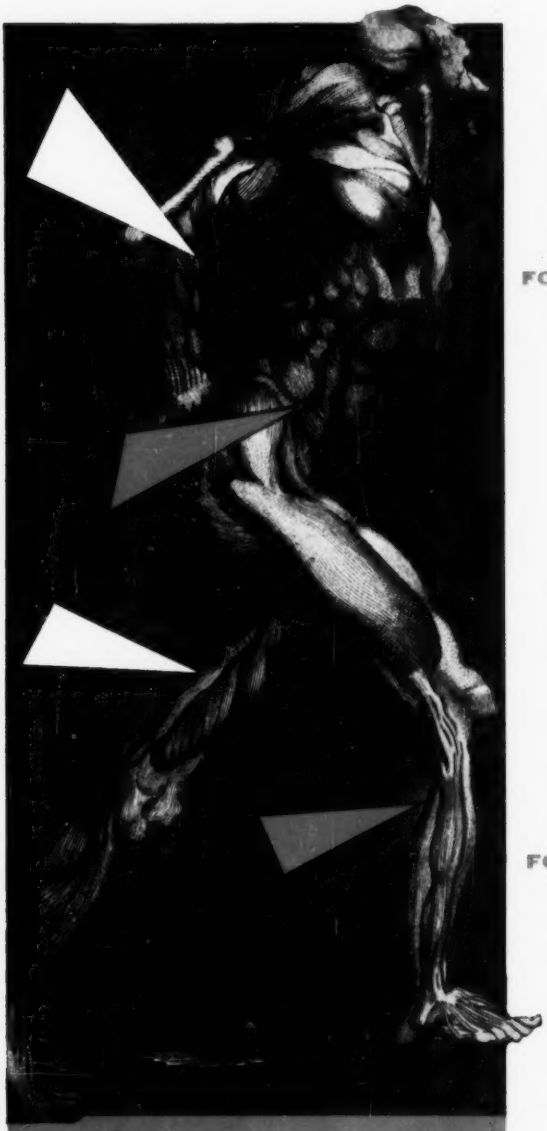

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